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Original Articles for October, 1958

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EDITORIAL

Keeping Up With Advances in Medicine

For clear, concise, or detailed reports about recent medical advances, the medical journal surpasses all other sources of information

JAMES M. NORTHINGTON, M.D., *Editor*

The decline of usefulness of the didactic lecture began with the invention of printing. When cheap paper became available and the linotype machine reduced the cost of typesetting by 75 per cent, the didactic lecture as a means of instruction lost much of its reason for being.

One of the eight surviving schools of the 45 medical schools originally chartered in New York announced at its opening 98 years ago that the lecture would have little place in its system of instruction. Today it appears that every medical school has followed that lead.

Medical men are greatly devoted to the tradition of conventions—gatherings where they can enjoy a meeting of the minds with their professional brethren. There is much to commend the custom, including good fellowship and a stimulation of professional interests. But how often do you read about architects, engineers, lawyers, teachers or members of any other profession getting together for a two- to five-day period for lectures to keep them informed on the practice of their professions?

Charles Darwin started out to become a doctor as his father was. But he became so disgusted with the teaching by lectures in the Medical School of Edinburgh University that he quit and went to Cambridge where he fell so much under the influence of the professor of botany as to cause

him to devote his life to natural history—very greatly to the advantage of human kind. John Stuart Mill and a host of others of the greatest scholars of the world have declared against the spoken, and in favor of the written, word as a means of teaching.

We have had anesthetics for only 115 years, knowledge of bacteriology and antiseptic (later aseptic) surgery for some 80 years. Previously, surgery was limited to amputations—with a mortality of some 25 per cent—and repairs of "ruptures" which would not stay repaired. And medicine was so ineffective that Oliver Wendell Holmes, M.D. (c. 1855) declared, "If the whole pharmacopeia were sunk to the bottom of the sea, it would be much the better for the human race, and much the worse for the fishes."

Medical meetings in those times were held infrequently and were devoted mostly to efforts at keeping down competition from irregulars. When ether and antiseptic surgery made invasion of the abdomen possible, the forward-looking promoted meetings to make the new knowledge known to the lesser brethren and to let it be known that the new "Listerism" was available for their use. With the marvelous discoveries in medicine and the multiplicity of specialties and hospitals, more and more "reasons" appeared for more and more gettings together.

In listening to a lecture it is inevitable that a sentence here and there will be lost, and so possibly will the whole of the rest of the lecture. Reading it in a journal, the word or sentence lost or obscure may be cleared without loss of time. Moreover, the journal remains for later reference. A further advantage of reading the article in a journal is that the reader gets the article in improved form since it has come under the critical eye and been subjected to the busy pencil of the editor.

Few doctors will need to be reminded of the time they have wasted while some celebrity discoursed on some obscure condition he had encountered (or heard about) of such rarity as to make it unlikely that one case would be seen in a whole lifetime of general practice.

In a journal carrying the meat of articles published all over the world on disease conditions one will *probably* encounter, and enough on those one will *possibly* encounter or *probably* be asked about to keep the reader from appearing to be behind the times, 90 per cent of the doctors in our country will find all their patients need for them to know, which is far more than can be said for listening to lectures at medical meetings.

So go to medical meetings whenever you can. But look upon them as a place to meet and cultivate friendships among your colleagues, as a place to view interesting exhibits, to see new instruments and appliances. Also as a place to learn new methods by listening to the lectures without feeling that you simply must get every word or phrase at the time. Rest assured that your favorite medical journal will furnish you with all the details later.

Finally, go frankly for the recreation it affords to be away from your usual duties, your hospital, your office, and the nagging necessity to observe details. Get the broad view of the meetings and be certain that the worthwhile details will be at your disposal in the next issue of your favorite medical journal.◀

ORIGINAL ARTICLE

The Use of Cortico-steroids in the Treatment of Allergic Diseases

Used judiciously, cortico-steroids are valuable adjuncts in the treatment of numerous allergic conditions

EARL B. BROWN, M.D., F.A.C.P.,* *New York, New York*

For ten years the corticoids have been used successfully in the treatment of allergic patients and have allowed the rehabilitation of patients who otherwise might be severely incapacitated. Others with milder allergic symptoms have led more comfortable and hence more useful lives.

Since the advent of cortisone great progress has been made in synthetizing new compounds which are more potent milligram for milligram, culminating in the newest methylprednisolone and triamcinolone. Fortunately this increase in potency was accompanied by a decrease in unwanted side reactions. There is no longer need to place patients on salt-free diets or add supplemental potassium to the diet. The dangers of gastrointestinal distress such as ulcer and/or perforated intestine have been reduced but not eliminated. Since the cortico-steroids are not cures but only powerful agents for symptomatic relief, these drugs should not be used in situations where medications with less toxic effects will serve the purpose.

*From The Institute of Allergy, The Roosevelt Hospital.

POLLENOSIS

Mild pollenosis can usually be con-

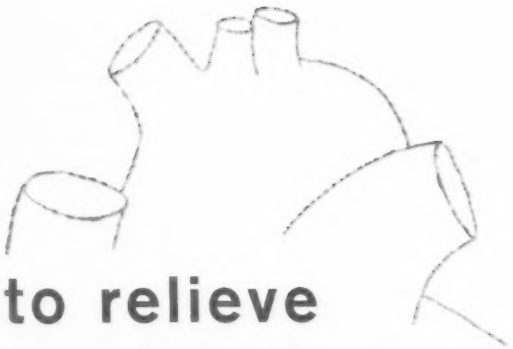
trolled by one of the antihistaminic preparations. In patients with severe symptoms it may be necessary to use cortico-steroids. Combining antihistamine with prednisolone serves no useful purpose. One of these preparations contains 2.5 mg. of prednisolone. This amount given four times a day alone should control the symptoms in cases of mild pollenosis. A double blind study comparing the effectiveness of small doses of cortisone plus antihistamine with both cortisone alone and the antihistamine alone was made in 1952.[1] This study was repeated in 1953,[2] substituting hydrocortisone for cortisone. In neither case was the combination found to be more effective than the steroid alone. A danger in prescribing the combination is that there is a tendency to assume that one is using just another antihistamine and does not exercise the usual precautions as when using a steroid. All patients should be encouraged to undergo hyposensitization with the specific pollen in their immediate area. Only those patients who are seen co-seasonally and do not respond to the antihistaminics or related symptomatic relief should be treated with corticoids. Prednisolone in doses of 10 to 20 mg. daily for 2 to 3 weeks should suffice. The newer steroids are administered in 20 per cent smaller doses. If a patient who has taken the cortico-steroids should suffer a constitutional reaction due to overdosage of the pollen, the symptoms are apt to be much worse than if he had received no cortico-steroids. In addition to the usual methods of controlling the reactions — epinephrine and applying tourniquets—intravenous soluble hydrocortisone may be necessary.

1. Brown, E. B., & Scideman, T., *J. Allergy*, 24: 364,1953.
2. Unpublished data.

BRONCHIAL ASTHMA

It is in this wheeze-cough-dyspnea syndrome that the greatest misuse of the cortico-steroids in allergy is likely to be found. The author has seen it used in cases of bronchogenic carcinoma, tuberculosis, heart failure and acute bronchitis which were referred to as "asthma." No attempt had been made to establish a diagnosis before prescribing the medication. The doctor who ever bears in mind the truism, "all that wheezes is not asthma," will never make this mistake.

The use of cortico-steroids in acute status asthmaticus should be prompt and in adequate dosage. It must be remembered that there is a 24- to 48-hour lag before the oral medication becomes effective. If the symptoms are very severe, the patient should be given *either* 20 units of ACTH *or* 100 mg. of water-soluble hydrocortisone in 500 cc. of 5 per cent glucose in distilled water, by slow intravenous drip, to last six hours. This can be repeated two to three times per day until the oral medication has become effective. Once the initial infusion has been started, prednisolone 10 mg. can be given orally and repeated every six hours. This dose should be given for 48 hours and then gradually decreased, usually by 10 per cent every 48 hours, as the condition improves. Occasionally it is necessary to increase the starting dosage by 25 per cent, but if the patient does not respond to 60 mg. per 24 hours, further increases are valueless. While using the steroids, the bronchodilators, expectorants and antibiotics should not be neglected. As the steroid dosage is reduced the bronchodilator dosage should be increased. However, since the cortico-steroids will not interfere with skin-testing while the bron-



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chodilators may, the latter are not used if it is intended to carry out this form of investigation. The patient is apt to feel much better after 36 to 48 hours of cortico-steroid therapy. However, the chest may not be clear for 10 to 12 days after a severe asthmatic episode. The reduction in dosage should be guided slowly by what one hears by the stethoscope.

It is necessary to maintain indefinitely on prednisolone or methylprednisolone the few patients who without this medication would be bed-ridden invalids. Maintenance dosage can be as low as 2 to 4 mg. daily of methylprednisolone, 20 per cent higher of prednisone or prednisolone. These patients should be seen weekly or every second week at which time interval history concerning any side reactions should be elicited. The use of steroids intermittently is preferred, and frequently it is found that one or two courses a year will keep severe asthmatics comfortable, with the judicious use of bronchodilators or expectorants between courses. For a patient unable to go a week or two without the steroids, maintenance dosage may be preferred. Adrenocorticotropic hormone should not be used in conjunction with the oral cortico-steroid except as already discussed.

PERENNIAL ALLERGIC RHINITIS AND NASAL POLYPS

Many patients are seen with perennial nasal obstruction which may or may not be accompanied by sneezing and rhinorrhea. Frequently nasal polyps, a result of the long-standing allergy, add to the discomfort. Symptomatic relief is afforded by the dosages used for bronchial asthma.

As the steroids will not interfere with the diagnostic skin test while the antihistaminics may, they are preferable for short-term treatment. In many cases polyps will shrink while the patient is receiving corticoids, but will immediately return to their previous size when the drug is discontinued. If the sinuses show evidence of infection the polyps should be removed, the infection treated, and adequate allergic management instituted.

There rarely is indication for long-term use of the steroids in this group of patients. For the occasional patient whose disease can not be controlled because of failure to find the cause of the difficulty, small doses of the steroids, 2 to 5 mg. daily, will control the symptoms and is preferable to the constant use of nose drops or nasal sprays which in the long run will do much harm.

ALLERGIC DERMATOSES

This group covers a wide range of miscellaneous skin ailments:

1. Atopic Eczema: The oral steroids are to be used only initially in the severe cases to control the cruel itching and thus stop the scratching. For infection resulting from the scratching, suitable antibiotic therapy should be added. If the cause of the eczema can be found and removed, steroid therapy will not be necessary. In case the etiology is obscure and symptoms persist, *topical* steroid therapy is preferable and usually adequate. There are cases which can be controlled only with oral steroids. After initial control, doses as small as 5 mg. two or three times a week may suffice.

2. Acute Urticara, Acute Angio-Edema, and Acute Contact Dermatitis: In this group of patients in which symptoms are self-limited, the cortico-steroids have their greatest use in allergy. The symptoms are due to the

DOSAGE SCHEDULE FOR RELIEF OF ADULT PATIENTS WITH ONE OF THE FOUR MAJOR ALLERGIC SYNDROMES

Allergic Syndrome	Initial Dosage		Maintenance Dosage	
	Prednisone or Prednisolone	Methylprednisolone or Triamcinolone	Prednisone or Prednisolone	Methylprednisolone or Triamcinolone
Bronchial Asthma	10 mg. 4 x daily for 48 hours	8 mg. 4 x daily for 48 hours	5 mg. 2-3 x daily	4 mg. 2-3 x daily
Seasonal Allergic Rhinitis	15-20 mg. daily for 2-3 weeks	12-16 mg. daily for 2-3 weeks		
Perennial Allergic Rhinitis	10 mg. 4 x daily	8 mg. 4 x daily	5-10 mg. 2-3 x daily	4-8 mg. daily
Allergic Dermatoses	30-40 mg. for 3-4 days	24-32 mg. daily for 3-4 days	2.5 mg. daily to 5 mg. twice weekly	2 mg. daily to 4 mg. weekly

ingestion of some food or drug, or contact with some substance, to which the patient is sensitive. Penicillin reactions and poison ivy are examples. Since the symptoms are self-limited, only short-term therapy is necessary. Patients should be given 40 mg. of prednisolone or 32 mg. of methylprednisolone for 24 hours, then the dose reduced as indicated by symptoms, for a five- to seven-day course.

3. Chronic Urticaria: The steroids are generally ineffective in this disease, even in the higher dosages such as 30 to 40 mg. daily. Very rarely is there response to lower doses. The dangers inherent in giving the steroid medication in high doses over long periods of time contraindicate their use in cases of chronic urticaria.

4. Chronic Contact Dermatitis: The etiological agent is usually obscure and these patients could be handled as summarized under atopic eczema.

5. Migraine: Some patients who have received the cortico-steroids for allergic disease have had relief of migraine when ergotamine did not work.

DISCUSSION

The newer steroids have an advantage over cortisone and hydrocortisone as patients do not usually require salt-free diets or supplementary potassium. The danger of gastrointestinal symptoms still persists. Moon-face, urinary frequency, excessive stimulation of appetite are all side reactions which are completely reversible. The use of the steroids may lead to exposure of a latent diabetes which if mild can be controlled by diet and will disappear when the patient discontinues the corticoids.

The same precautions should be taken as when using the older steroids. There are no absolute contraindications in the use of the steroids. It is presumed that if the cortico-steroids are used in cases of tuberculosis, diabetes, psychosis, hypertension or gastrointestinal dysfunction coexisting with the allergic syndrome, the allergy is more dangerous to the well-being of the patient than the diseases named. The patient in these circumstances should be hospitalized and close supervision should be maintained. Medications such as streptomycin, p-aminosalicylic acid or isonicotinic hydrazide for tuberculosis, insulin for diabetes, tranquilizers for psychoses, anti-hypertensives and anti-acids may all be given with the steroids.

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Current Concepts in Therapy: Sedative-Hypnotic Drugs II. Chloral Hydrate. New England J. Med. 255:706 (Oct. 11) 1956.

Adults: 1 or 2 7½ gr. capsules or 1 or 2 teaspoonfuls of Noctec Solution 15 to 30 minutes before bedtime.

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In otherwise normal patients the short-term use of steroid (2 to 3 weeks) carries very little hazard. Patients on long-term therapy should be seen weekly or every other week, and be instructed to call the physician at the first evidence of any unusual symptoms.

Since the adreno-corticotropic hormones act through the adrenal gland only, they should be used in conjunction with the oral medication. Once a patient has been under the stimulus of adequate cortcio-steroid therapy, the adrenals will not respond to this hormone, because of either cortical atrophy or loss of sensitivity to the pituitary hormone. If it is desired to quickly raise the cortisone level of the blood, intravenous hydrocortisone is indicated.

Any time after six months following the last course of high dosage and prolonged steroid therapy, a patient undergoing a stress situation such as major surgery, infection or severe emotional trauma should be given supportive cortico-steroids. The time in which a patient's adrenals will respond to endogenous hormones varies with the amount of cortico-steroid consumed plus duration of therapy. As there might be a lag of 48 hours for the oral medication to take effect, intravenous or intramuscular cortico-steroid may be desirable.

In conclusion the cortico-steroids are a potent force for alleviation of allergic disease, but all patients with allergies do not need this treatment. Many who are receiving it would fare much better with adequate allergic management. All patients presenting themselves with allergic symptoms should be subjected to an intensive allergic diagnostic survey. Under no circumstances should cortisone be prescribed or used where this has not been done or is not contemplated.◄

ORIGINAL ARTICLE

The Office Treatment of Cardiovascular Debility

A simple, effective regime for treating mild cardiovascular disease in older patients is described

THOMAS J. VISCHER, M.D., *Philadelphia, Pennsylvania*

The steady lengthening of human life causes a great increase in the number of cases of somatic and mental afflictions so frequent in old age. The literature is replete with reports on the results achieved with analeptic, tranquilizing, antihypertensive, relaxing and sedating drugs in patients suffering from greater or lesser physical and mental disability. Many such reports deal exclusively with the institutionalized.

OUT-PATIENTS

For every one such patient there are many older, as well as younger, whose physical and mental status, while not in need of drastic therapy, needs sympathetic attention and suitable medication. Many such persons have disability of a cardiovascular nature and some impairment of memory. Many of these patients have lost all ambition and submissively bear the afflictions of their disablement. It is the duty of doctors to stimulate and sustain the remaining capabilities of these patients so as to make their remaining years—often many—as interesting and pleasant as possible. Physicians who care for the elderly will be called upon more and more to treat "chronic myocarditis," threatened cardiac failure with congestion, hypertension, arteriosclerosis and similar lesions, with and without renal complications. There may be no more than a general weakening of muscular

strength in which the heart muscle also is involved, slight dyspnea on moderate exertion and some edema of the ankles, particularly toward the end of the day. Many other patients have arteriosclerotic heart disease with or without hypertension, incipient cardiac decompensation, angina pectoris, myocardial infarctions, general arteriosclerosis, chronic bronchitis, asthma, diabetes, and neuroses.

Treatment of the average patient with less severe lesions may be assumed to last a long time, often for many years, and a therapy is indicated which is effective, yet simple and safe. Almost always, except for acute exacerbations, oral therapy is the treatment of choice since this route of administration will, to a great extent, rid the patient of the continual dependence upon his physician for injections or other specialized therapy. Proper physical and mental hygiene, diet, controlled exercise, tonics, vitamins, cardiotonics, vasopressors or vasodilators, diuretics, insulin, and/or analgesics may be indicated at one stage or another.

Overweight puts an additional strain on the gradually weakening heart and increases the dyspnea. Advancing age with arteriosclerotic changes will reduce circulatory efficiency and, by involving the intracranial vessels, will reduce the function of the respiratory and circulatory centers, and often impair mental processes. Coronary narrowing will curtail the oxygen supply of the myocardium. The kidneys will have a decreased blood supply. It is inevitable under these circumstances that angina of effort, increasing edema, and cardiac changes frequently develop.

TREATMENT OBJECTIVES

Therapy, to be effective, must improve the blood supply of the heart by dilating the coronary arteries, improve the action of the heart muscle, and rid the patient of excess tissue fluid.

Digitalis is still the most useful cardiotonic, but it is toxic and has many undesirable side effects such as bradycardia, coronary constriction rather than dilation, etc. As diuretics, the mercurials lead the field, but they, likewise, are toxic and, if not carefully controlled, lead to sodium depletion and electrolyte imbalance, while long continued use involves the risk of kidney damage.

THE XANTHINES

The xanthines have proved to be the safest and most effective medicaments for cardiovascular disease, especially when treatment must be continued for years. The xanthines are underrated; their amply-proved beneficial effects in the past have been obscured in the light of new drug developments. They produce coronary dilation,[1] stimulate the heart muscle, increase stroke volume, cardiac output and work,[2] and, though not such potent diuretics as the mercurials, are efficient in the treatment of cardiac edema, and they do not lead to excessive sodium loss.[3] The xanthines will also be of value in those cases where glomerular filtration rate is very low.[4] Here the tubular epithelium will be in contact with the filtrate over long periods of time, allowing reabsorption of more salt and water. In such cases the effectiveness of the mercurials will be reduced and the circulatory action of the xanthines

1. Barnum, D. R., et al., *Quart. Bull., Northwestern Univ. M. Sch.*, 24:6-11,1950.
2. Beckman, H., Pharmacology in Clinical Practice, W. B. Saunders Co., Philadelphia, 1952.
3. Schroeder, H. A., *Circulation*, 4:87-99,1951.
4. Schroeder, H. A., *J.A.M.A.*, 147:1109-1118,1951.

A CIBA Documentary Report

How clinicians evaluate the safety and effectiveness of RITALIN® as a psychic stimulant

CONDITIONS TREATED	RESULTS	COMMENTS ON SAFETY
Depression accompanying chronic illness and convalescence from short-term illness; mild depression induced by life pressures; overtranquilization.	"The drug gave a plateau type of stimulation, smooth onset, with no euphoria . . . The effect lasted about four hours, gave the patient a feeling of well-being . . ."	"The side effects of Ritalin are minimal." "The work showed that the drug had no effect on blood pressure, the blood count, urine or blood sugar, did not depress the appetite, and produced no tachycardia."[1]
Lethargy, fatigue and emotional depression secondary to chronic illness in elderly patients; mild depression secondary to short-term illness. (Twenty-three "normal," healthy people also received the drug.)	"For the entire 112 patients 66 per cent showed marked improvements [obvious drug effect and mood improvement] . . ."	"No serious side reactions were noted . . . In no case was it necessary to stop the drug. No evidence of significant effect upon blood pressure or pulse has been found. This is particularly interesting, since these side effects have been common with other mood elevating drugs . . ."[2]
Drug-induced psychophysiologic depression; physiologic after-effects of certain anesthetics; barbiturate intoxication; moribund states due to systemic infection. (All patients were epileptic, mentally retarded and/or brain damaged.)	"All except two [of 129] patients responded to the initial injection [of parenteral Ritalin] within 1½ to 15 minutes."	"In no instance was there any evidence of untoward effects." ". . . the very poor basic physical condition of our patients in this study, those associated with profound chronic brain damage, accentuates the safety of parenteral Ritalin . . ."[3]

DOSAGE: *Oral:* Dosage will depend upon indication and individual response. Many patients respond to 10 mg. b.i.d. or t.i.d. Others will require 20-mg. doses. In a few cases, 5-mg. doses will be adequate. If inability to sleep is encountered, last dose should be given before 6 p.m. *Parenteral:* 10 to 30 mg., intravenously or intramuscularly.

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References: 1. Natenshon, A. L.: Dis. Nerv. System 17:392 (Dec.) 1956. 2. Landman, M. E., Preisig, R., and Perlman, M.: J. M. Soc. New Jersey 55:55 (Feb.) 1958. 3. Carter, C. H., and Maley, M. C.: Dis. Nerv. System 18:146 (April) 1957.

CIBA SUMMIT, N. J.

might represent the one factor needed to enhance diuresis while continuing mercurial medication. Furthermore, the xanthines can be given in kidney lesions when mercurials are contraindicated.

To avoid gastric irritation, a slowly soluble calcium salicylate salt of theobromine has proved eminently satisfactory.[5] In contrast to the more soluble theobromine compounds, it is well tolerated by the stomach, does not lead to tolerance, and may be given continually for years.

From 30 years' experience in internal medicine, 112 case histories have been chosen as representative of the many hundreds of patients seen suffering from one or more of the various forms of cardiovascular disease, arteriosclerotic heart disease, and general arteriosclerosis, with or without hypertension, angina pectoris, coronary occlusion, so-called chronic myocarditis, valvular heart disease alone or in various combinations. The ages of these patients varied from 35 to 88 years, with a mean age of 65 years. Treatment frequently lasted for many years and during this time those who first came suffering from symptoms more or less typical of their various lesions, were not only kept comfortable by medication, but were in many instances able to live useful lives. In one-half of these such medication consisted almost exclusively of *Theocalcin* in doses of 1 or 2 tablets three or four times a day. All patients had at least yearly check-ups, including blood counts and blood chemistry examinations. There were no detrimental effects attributable to the xanthine medication, even when such therapy was continued for many years. Edema, when present, was always reduced. In most cases, despite the advancing age of these patients, blood pressure readings were lowered, at least to a degree.

*Theocalcin®, Knoll Pharmaceutical Company, Orange, N. J.

5. McCombs, R. P., Internal Medicine: A Physiologic and Clinical Approach to Disease, Chicago, Year Book, 1956, p. 64.

ADJUVANTS

Some patients received other xanthines; aminophylline or *Phyllicin*, and, at times, mercurial diuretics. Cardiac decompensation, actual or threatened, was treated with digitalis, some patients regularly receiving 1/10 mg. of digitoxin as long as indicated. Insulin was given in diabetes, cortisone for painful arthritic lesions, etc. Terminal cancer pain was alleviated with opiates.

CEREBRAL OR CORONARY ATTACKS

While death in the patients who finally expired was, except for intercurrent disease, usually due to cerebral hemorrhage, coronary sclerosis, or general asthenia with myocardial weakness, it seems noteworthy that very few of those given xanthines had intercurrent attacks of cerebrovascular hemorrhage, "little strokes," or cononary occlusion—conditions so common in this type of case that they may be said to be expected. Of such complications that did occur, recovery was in many cases astonishingly rapid. It does not seem over-optimistic, in view of the pharmacologic actions of the xanthines, to attribute some protective action to these drugs.

CASE REPORTS

Case 1

A woman of 55, first seen February, 1937. *Diagnosis:* Arteriosclerotic heart disease. Blood pressure 190/120. Complained of precordial distress with occasional pain on exertion, nervousness and vertigo. *Physical findings:* Extremely tense, but without evidence of distress. Lungs negative.

Heart showed an exaggerated A-2, no murmurs. Apical rate 88. *Laboratory findings:* B.M.R. minus 26, blood sugar 100, blood urea 8, blood cholesterol 137.5. Sedimentation rate 20, hematocrit 48, r.b.c. 4,550,000, w.b.c. 6,400, hb. 13 grams.

When last seen in July, 1956, blood pressure was 170/90, the patient felt well and had no complaints. She had been taking *Theocalcin* and phenobarbital since February, 1937.

Case 2

A woman of 70, first seen November, 1945. *Diagnosis:* Arteriosclerotic heart disease. Complained of nausea and abdominal distension, sensation of syncope with precordial distress. *Physical findings:* No apparent distress. Lungs negative. Apical rate 72. Blood pressure 170/110. *Laboratory findings:* B.M.R. minus 20, urine negative, blood sugar 112, blood urea 5, cholesterol 162.5, sedimentation rate 16, hematocrit 51, r.b.c. 4,920,000, w.b.c. 6,200, hb. 14 grams. E.C.G. normal.

Last seen July, 1956. Patient has been taking *Theocalcin* and phenobarbital since November, 1945. No complaints. Blood pressure 140/80.

Case 3

A woman of 72, first seen September, 1948. *Diagnosis:* Generalized arteriosclerosis, hypertensive heart disease. Complained of shortness of breath and headache. *Physical findings:* Overweight, 195 lbs. Lungs negative, blood pressure 180/120. Apical rate 72. No murmurs, normal rhythm. *Laboratory findings:* B.M.R. minus 4, sedimentation rate 22, blood sugar 92, blood urea 7, cholesterol 137.5, hematocrit 52, r.b.c. 4,510,000 w.b.c. 4,500, hb. 14 grams. E.C.G. normal. Fluoroscopy showed a general moderate enlargement of the heart.

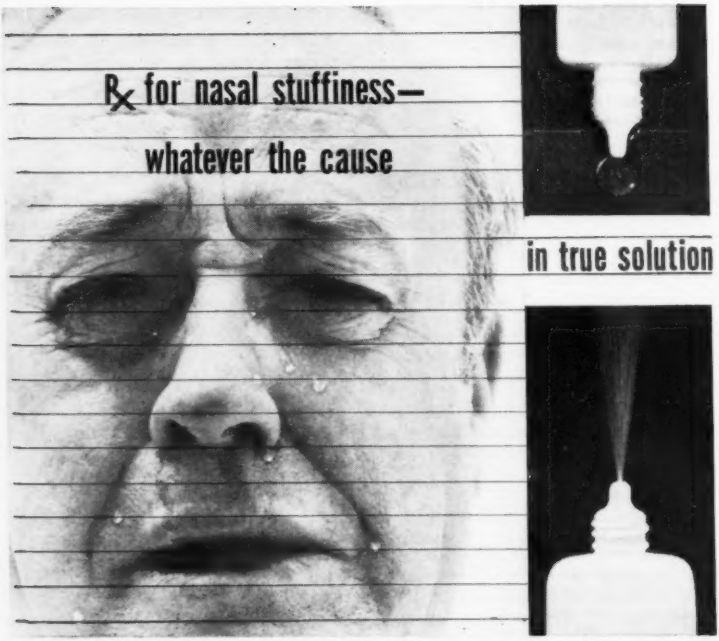
When last seen in July, 1956, blood pressure was 140/90, patient had no complaints. Weight remained at 195 lbs. Patient has been taking *Theocalcin* with phenobarbital for the past 8 years.

DISCUSSION

When this evaluation of case histories was begun, those selected were of patients followed clinically until death after 1 to 19 years. The age of these patients (8 men and 14 women) when first seen was from 50 to 88 years, mean age 68 years. Their mean age at the time of death was 74 years. Several of them then were over 90 years old. All of these individuals were treated as outlined above. The purpose of this report is to show that persons suffering from various cardiovascular lesions can be made comfortable and kept so by simple, safe forms of therapy of which the much-neglected xanthines are the mainstay in the author's therapeutic armamentarium. Certainly, more serious cardiac lesions require more strenuous therapeutic measures, but for the milder lesions it would be hard to find any other form of treatment so free from side effects and complications. At most, some nausea may temporarily halt the xanthine therapy for a few days. Usually this will disappear shortly or can be overcome by giving the medication with, or directly after, meals or by reducing the dosage.

SUMMARY

By using slowly soluble xanthine salts such as theobromine calcium salicylate (*Theocalcin*), theophylline calcium salicylate (*Phyllicin*), or similar non-irritating xanthine salts, many older patients can be kept comfortable and lead useful lives for their remaining years.◀



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*DOSAGE: as spray—2 sprays into each nostril every 2-3 hours.
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Direct-Vision Intracardiac Surgery

With the new direct-vision techniques, intracardiac surgery may become an elective rather than an imperative measure

FREDERICK S. CROSS, M.D., *Cleveland, Ohio*

The future of cardiac surgery lies in the continued development of safe direct-vision techniques. The advantages of the open techniques are obvious:

1. Easy visualization of all valves, septa, and chambers.
2. Complete correction of existing defects when possible.
3. Identification and repair of previously undiagnosed associated defects.

It has become evident that the acquisition of a satisfactory heart-lung machine fills only one of the basic requirements for successful, direct-vision intracardiac surgery. The others involve accurate preoperative physiological investigation of the patient, intensive experience in perfusion methods, perfection of intracardiac surgical techniques, and an appreciation of new problems in anesthesia as well as associated clinical problems, especially in the immediate postoperative period.

Many pump oxygenator systems have been devised. Probably the most widely used are various modifications of the bubble-type oxygenator of DeWall, the Gibbon-type pump oxygenator, and the rotating disc, reservoir oxygenator which is finding increased popularity at the present time. The latter two oxygenators are referred to as "filmers," in that a thin film of blood is exposed to the oxygen atmosphere. Still another type is the mem-

brane oxygenator, the blood and oxygen being separated by a thin plastic membrane. This type is just coming into clinical use.

PERFUSION TECHNIQUES

Perfusion techniques are the many complicated and integrated procedures necessary for the operation of the heart-lung machine in order to carry the patient through surgery successfully. Perfusion rates of 50 to 120 cc./Kg./min. have been used, but the general range is 60 to 80 cc./Kg./min. During the period of bypass all important events such as mean arterial blood pressure, central venous pressure, the electrocardiogram, and the electroencephalogram are monitored. In addition, blood is drawn at 15 minute intervals to be analysed for oxygen and carbon dioxide content, pH, platelets, and hemolysis. An attempt is made to maintain the mean arterial blood pressure above 60 mm. of mercury. It may be necessary to add a vasopressor to the circulating blood to accomplish this. The adequacy of the blood flow is determined by the mean arterial blood pressure as well as the brain wave pattern in the electroencephalogram.

Blood balance must be maintained accurately during and immediately after the perfusion. To accomplish this the patient is weighed immediately pre- and post-operatively, and the weight adjusted accordingly if necessary. During the perfusion the degree of congestion of the conjunctival vessels is continuously observed. In addition, all blood loss from, as well as blood added to, the perfusion system is recorded. By rigid attention to all these details, prolonged perfusions, well tolerated by the patient, are possible. Our longest successful perfusion to date has been one hour and 55 minutes.

INTRACARDIAC TECHNIQUES

The heart is exposed in most instances by a trans-sternal incision made through the fourth interspace bilaterally. A dry operative field is mandatory for proper identification and repair of intracardiac defects. This has been obtained most frequently by means of a sump-type suction tip in the heart connected to a line returning the coronary sinus blood to the oxygenator. Potassium citrate-induced cardiac arrest has been used electively only in those instances in which the defect is difficult to visualize, or in which there is a great deal of blood regurgitating through the defect to hinder proper visualization. As more experience is gained, elective cardioplegia is becoming a safer and more valuable adjunct to open cardiac surgery.

The greatest experience to date has been in the repair of ventricular septal defects, auricular septal defects, and pulmonic stenoses existing alone or in various combinations. Ivalon sponge prostheses have been used in the repair of the larger ventricular septal defects, some of the smaller defects have been closed by interrupted sutures only. Atrial septal defects are closed by direct suture using continuous sutures of OOO silk on an atraumatic needle. The continuous suture may be reinforced with interrupted sutures. Pulmonary stenosis has been approached either through the right ventricle or through the pulmonary artery. It is believed that the approach through the right ventricle is advantageous because other defects such as an associated infundibular stenosis or a ventricular septal defect

can be identified easily and repaired if present. It is a simple task to correct pulmonary stenosis through either approach by cutting the stenotic valve along fused commissures and then cutting off the fibrous tip of the funnel-shaped valve if necessary.

PHYSIOLOGICAL DATA

As mentioned previously, physiological data are obtained on all patients before, during, and immediately after open intracardiac surgery. Emphasis is placed on the importance of such physiological studies, for it has been through the analysis of these data that the techniques for direct vision surgery have been continually refined. With the blood flow rates utilized, occasionally supplemented with vasopressors, it is easy to maintain a mean arterial blood pressure of at least 60 mm. of mercury. The clotting mechanism of the blood has not been disturbed. The clotting time is returned to less than 15 min. by giving protamine sulphate in a dose calculated to be one-half to three-quarters of the initial heparin dosage. In most instances, platelet counts remain above 120,000, dropping to about one-half of the preoperative level. There has been no significant change in plasma fibrinogen or clot lysis. Blood destruction has been minimal with only slight increases in the plasma hemoglobin during the period of cardiac bypass. Usually the arterial oxygen saturation is maintained above 95 per cent, and the pH has been between 7.35 and 7.45. Blood balance is well maintained during the operative procedure in that postoperative weights are always within a quarter of a pound of the preoperative weight.

RESULTS

As in all new or developmental surgery, mortality started high and has gradually improved as techniques have been improved. Overall mortality in the early experience of those cardiac surgeons obtaining the best results was in the vicinity of about 25 per cent. The general mortality has dropped to 10 per cent, and recently at least three groups of cardiac surgeons have reported a series of 30 to 40 consecutive operations with no mortality. It is perhaps not fair to speak strictly in terms of general mortality since many patients operated upon are either hopeless risks or have anatomical defects difficult or impossible to repair. At the present time the mortality for a single uncomplicated defect—such as of the ventricular septum, an atrial septal defect, or pulmonic stenosis—is approaching zero. We have reported a series of 80 single uncomplicated defects with one death. Likewise, as experience is gained, the morbidity associated with direct vision surgery utilizing the pump oxygenator is decreasing. With increasing experience, the incidence of pulmonary complications and postoperative bleeding as well as other complications is gradually decreasing.

Of great importance in decreasing the total mortality and morbidity associated with open cardiac surgery is the establishment of special postoperative cardiac nursing units, with specially trained nurses of wide experience in the postoperative care of such patients. These recovery areas are equipped with all types of emergency equipment including thoracotomy setups, complete anesthesia equipment, a defibrillator, ECG machine, and all the emergency drugs. A rigid program of postoperative care has been worked out which minimizes the risk of surgery to these patients. Such at-

tention to the details of postoperative care has been a significant factor in improving survival rates in this type of surgery.

SUMMARY

The future of cardiac surgery lies in the further development of safer direct-vision techniques utilizing the pump oxygenator. With increasing experience morbidity and mortality is decreasing to respectable levels. In our experience, with few exceptions, good- to fair-risk patients with anatomical defects easy to correct have done well. It has been the poor-risk patient or the one with the complicated defect who has not survived surgery. This observation indicates that the time is here when many intracardiac defects can be viewed as a patent ductus arteriosus is viewed at the present time; that is, when the optimal time for surgery is reached, it is performed electively rather than waiting for the development of significant symptoms.◀

Sudden Death Related to Constipation

Vascular accidents and quick death may result from excessive bathroom straining. *Senokot* effectively and simply reduced the incidence of excessive straining. Straining may bring on extreme variations in blood pressure and circulation.

Selman, D., *Wisconsin M.J.*, 57:160,1958.

ORIGINAL ARTICLE

Effects of L-Glutavite Upon Memory Defects in Psychosis

Improved cerebral function and beneficial influence on memory recall, especially in geriatric patients, were obtained from this medication

JOSEF MATFUS, M.D., and JOSEPH H. KOENIG, M.D.,
Central Islip, New York

The elderly person with few family ties and fewer friends is a pathetic figure. Ignored or left to himself in homes of relatives or in an institution, he becomes increasingly listless and apathetic. Often he is labeled "senile" when he is only depressed. The practitioner is as much concerned with this patient as the institutional physician. Increasing emphasis is being placed on efforts to stimulate the mental function of these individuals along with the treatment of their organic disease.

In a study of the effect of the administration of large daily doses of monosodium L-glutamate in a series of senile psychotic persons, gratifying improvement in the mental states of a significant number of persons has been reported.[1] Previous studies have shown that it is a useful drug in the management of elderly persons suffering from fatigue, mental depression, and decline in mental function.[2-5]

1. Himwich, H. E., et al., *J. Nerv. & Ment. Dis.*, 121:40-49,1955.
2. Katz, E. M., & Kowaliczko, Z., *Internat. Rec. Med. & General Practice Clin.*, 169:9,1956.
3. Tourlentes, T. T., et al., *Illinois M.J.*, 112:121-124,1957.
4. Wolff, K., Personal communication.
5. Chu, J., The Use of "L-Glutavite" in Geriatrics, *J. Indiana M.A.*, 50:992-998,1957.

Patients receiving *L-Glutavite** have shown significantly greater improvement than those receiving other medications.[6] This study and other studies supporting the value of this medication prompted this clinical investigation.

METHOD AND PROCEDURE

Patients were selected from three different wards on the basis of similarity of memory defect and similarity of age. The 18 patients selected for this study were aged 41 to 88, only a few below 60. All were given five packets of *L-Glutavite* each day. with instructions to take two doses before breakfast, one before the noon meal and two before the evening meal.

The influence of the preparation upon memory was the chief concern and in order to measure the effect objectively, a psychometric test was used. The Wechsler Memory Scales (Form II) standard testing devices for memory with a good degree of reliability, were administered before initiating therapy. At the end of the three-month therapy period, the patients were then retested with Form I of the Wechsler Memory Scale. The same clinical psychologist administered both tests.

THE TEST GROUP

Of the 18 selected patients, 10 were diagnosed as psychotic due to alcoholic deterioration (Korsakoff's syndrome) all were institutionalized longer than three years, and eight were diagnosed as senile psychosis with general arteriosclerosis.

PROCEDURE

Before the administration of medication, the subjects were closely observed by the authors, attendants and nurses assigned to the wards. An assessment was made of the social adjustment and mental status of each patient. Form II of the Wechsler Memory Scale tests was then applied and the results recorded.

For the next three months each patient received five packets a day, in tomato juice or cold carbonated water. The only side effect noted was a brief redness of the skin which disappeared in less than 10 minutes.

At the conclusion of the therapy period, the patients were re-examined with Form I of the Wechsler tests.

RESULTS

Clinical findings: The patients seemed better able to concentrate and to care for themselves. There was a renewal of interest, and they became more socially aware. Their eating habits improved greatly. Group integration was favorably increased with lessening of patient apathy.

Psychometric evaluation: The tests indicated that recent memory was most affected. The ability to recall events of the recent past showed the most significant improvement, even where there was continued disorientation with regard to the past. Memory recall appeared to be augmented.

Seventy-two per cent of the patients showed some improvement in the follow-up examination by the Wechsler Memory Scales, most marked in patients with senile psy-

6. Barrabee, P., et al., *Postgrad. Med.*, 19:485-491, 1956.

*L-Glutavite,® Crookes-Barnes Laboratories, Inc., Wayne, N.J. Each packet contains: Monosodium L-glutamate 3.48 gm., Niacin 45.0 mg., Thiamine Mononitrate 0.6 mg., Riboflavin 0.8 mg., Ascorbic Acid 30.0 mg., Ferrous Sulfate 11.0 mg., and Dicalcium Phosphate 910.0 mg.

chosis, who definitely improved in their behavior, becoming more cooperative, more tidy, and better able to recall recent events. Four patients of the Korsakoff syndrome group showed significant improvement, four more demonstrated inconclusive results, and two became worse.

TWO CASE REPORTS

Case 1

A man of 51 years of age, was admitted to the hospital, and the diagnosis of psychosis due to alcoholism (Korsakoff's syndrome) was established. For the past two years, this patient has been observed by the same doctor. He was disoriented as to time and place, could not perform the simplest tasks involved in taking care of himself. He was an iron foundry worker who had completed the sixth grade at the age of 12. Upon comparing Forms I and II of the Wechlser Memory Scales, one is struck by the similarity of score obtained when judging personal and current information and general orientation. After three months of therapy, there was a decided improvement in the number of memories retained and recalled after reading the testing paragraphs, in ability to recall digits forward and backward, and in visual reproduction of figures. Upon retesting, the examiner noted that the patient now spoke clearly about his work. His orientation for time and place was good, and he was caring for himself adequately. His M.Q. on the Wechsler exams had increased by 10 points.

Case 2

A man, 66 years of age, was admitted to the hospital, with a diagnosis of chronic brain syndrome with arteriosclerosis. He knew neither the year, month, or day, nor that he was in a hospital. Following three months of therapy he knew the year and month, but not the day. He also knew that he was in a hospital and its location. He showed a 20 point improvement on the Wechsler scales, the most marked difference appearing in his ability at memory recall and digit retention.

RATIONALE OF THERAPY

Although a vast amount of study has indicated the fundamental role of glutamate in cerebral metabolism,[7] a definite explanation of its therapeutic effects in improving mental function is still lacking. Monosodium L-glutamate is effectively absorbed into the blood stream. After ingestion it appears in the circulation as glutamate.

Barrabee et al.[1] suggests three ways in which the preparation may be of help:

1. Enhancement of cerebral tissue metabolism by an optimal supply of glutamic acid.

2. Enhancement of enzymatic oxidation by an optimal supply of riboflavin, thiamine and ascorbic acid,

3. Enhancement of the effective vascular flow by the vasodilating influence of niacin aided by the hematinic action of ferrous iron.

SUMMARY AND CONCLUSION

Five packets of *L-Glutavite* were administered daily for 90 days to 18 patients at the Central Islip State Hospital. The Wechsler Memory Scale tests were employed in an attempt to objectively assay its effect upon memory.

There was general improvement of the patient's behavior and an increase in social activities. The patient was better able to concentrate and more capable of caring for himself.

Seventy-two per cent demonstrated improvement upon retesting with the Wechsler Memory Scales. Memory for recent events showed most improvement. The most marked improvements were seen in the patients with senile psychosis. Of the 10 patients with Korsakoff's syndrome, four demonstrated significant improvement.

After three months of therapy no significant side effects were observed.◀

7. Weil-Malherbe, H., *Physiol. Rev.*, 30:549-568, 1950.

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REFERENCES: 1. Carlozzi, M.: Ant. Med. & Clin. Therapy 5:146 (Feb.) 1958. 2. Welch, H.: Wright, W. W. and Staffa, A. W.: Ant. Med. & Clin. Therapy 5:52 (Jan.) 1958. 3. Marlow, A. A., and Bartlett, G. R.: Glucosamine and Leukemia. Proc. Soc. Exp. Biol. & Med. 84:41, 1953. 4. Shalowitz, M.: Clin. Rev. 1:25 (April) 1958. 5. Nathan, L. A.: Arch. Pediat. 75:251 (June) 1958. 6. Cornbleet, T.; Chesrow, E., and Barsky, S.: Ant. Med. & Clin. Therapy 5:328 (May) 1958. 7. Stone, M. L.; Sedlis, A., Bamford, J., and Bradley. W.: Ant. Med. & Clin. Therapy 5:322 (May) 1958. 8. Harris, H.: Clin. Rev. 1:15 (July) 1958.

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ORIGINAL ARTICLE

Dermatologic Therapy with New Analgesics

The use of several medications for the treatment of pruritus associated with dermatitis is discussed

CLARENCE SHAW, M.D., *Chattanooga, Tennessee*

Recent advances in the treatment of pruritis are responsible for placing improved preparations at our disposal.

Although members of the "caine" group of drugs, such as nupercaine and benzocaine, are efficient allayers of itching, they have the disadvantage of being frequent sensitizers. Because they are closely related chemically to many drugs in common use, *e.g.*, the sulfonamides, para-amino-benzoic acid, para-amino-salicylic acid, and paraphenylenediamine, there is sometimes a cross sensitization with these substances so that a person allergic to one may be allergic to others in the family.

REQUIREMENTS TO MAKE AN AGENT AN ANALGESIC

Any analgesic should have the following properties:

1. Frequently effective.
2. Cosmetically acceptable.
3. Minimal side effects.
4. Low index of sensitization.
5. Can be used over long periods of time.
6. Stable.
7. Inexpensive.

Local antihistamine preparations have failed to live up to expectations, and are frequently sensitizers, although when given by mouth or by injection they may help to allay itching, particularly in urticaria and drug reactions.

FOR RELIEF FROM PRURITUS

Among the most useful antipruritic agents are medicated baths. A colloidal oatmeal starch powder* added to the bath water is well tolerated and easy to use. Recently an oilated form has become available, which has advantage in patients with dry skin and is better tolerated in the cold months.

Colloidal oatmeal has also been combined with salts to form aluminum acetate† making an improved type of wet dressing for the relief of itching. Other valuable new wet dressing preparations are powders that combine colloidal soybean complex with salts,* and powders that contain both sodium propionate and chlorophyll.† The last preparation is not only bacteriostatic, but fungistatic as well.

THE CORTICOSTEROIDS

Certainly the most important new antipruritic agents are the corticosteroid drugs. Although cortisone itself is ineffective topically, hydrocortisone, fluorohydrocortisone, and prednisolone are remarkably efficient when applied to itching surfaces. Many reports[1] attest to the value of these substances indicating that hydrocortisone and related compounds are the most consistently successful antipruritic agents now available for topical use. There is evidence that fluorohydrocortisone can be absorbed in sufficient amounts to produce undesirable systemic effects; therefore it should be used only on small areas. There is little difference in value between the topical use of hydrocortisone acetate and hydrocortisone-free alcohol in ointment form. It is also apparent that 0.5% to 1% hydrocortisone ointment is adequate for most patients. The added expense of the 2.5% preparations is not justified. It is sometimes more economical to use these drugs systemically, especially in acute, self-limited, widespread dermatoses such as drug reactions, severe dermatitis venenata, and erythema multiforme. A few injections of ACTH followed by hydrocortisone, prednisolone or other similar compounds by mouth will frequently be sufficient to keep the patient with an acute dermatitis comfortable until the eruption has run its course. In chronic dermatoses such as eczema, neurodermatitis, psoriasis and others, they should be used with great caution since there is frequently a rebound with augmented pruritus when the drug is discontinued.

STILL ANOTHER MANNER OF USE

The corticosteroids are useful in another manner for analgesia. It has been shown that when a few drops of a suspension of cortisone or hydrocortisone are added to an injectible which is ordinarily painful, there is substantial reduction of discomfort.[2] It is a useful technique to employ in those patients who receive daily injections of any drug where eventually the site of injections becomes sensitive and indurated. Hydrocortisone can be injected directly into chronic, thickened, pruritic plaques of eczema and lichen planus sometimes with remarkable relief of itching.[3]

FOR LOCAL ANESTHESIA AND ANTISEPSIS

Recently, using pressure with an

*Aveeno®, Aveeno Corporation, New York.
†Bur-Veen®, Aveeno Corporation, New York.
*Soyboro®, Dome Chemicals, Inc., New York.
†Prophyllin®, Rystan Company, Inc., Mount Vernon, New York.

1. Noojin, R. O., *M. Clin. North America*, 565-573, 1957.
2. Cornblett, T. & Benjamin, F. B., *A.M.A. Arch. Dermat.*, 69:688-693,1954.
3. Savitt, L. E., *A.M.A. Arch. Dermat.*, 76:780-782, 1957.

ice cube containing benzalkonium chloride* has been suggested as a method for obtaining anesthesia with antisepsis.[4] Four cc. of a stock solution of the commercial concentrate of benzalkonium chloride is added to 50 cc. of water with a few drops of a dye such as gentian violet, Parker 51 ink, or methlyene blue, and poured into a standard refrigerator ice tray. This makes 14 ice cubes of 1:1000 solution. The patient holds the ice cube with a paper towel against the area to be anesthetized for 15-30 seconds, and so produces sufficient anesthesia for desiccation. It is particularly useful when injections of a local anesthetic would obliterate landmarks, as in spider angiomas, sunburst varicosities on the thighs, etc. It is also recommended for children and adults who are needle-shy.

4. Zimmerman, M. C., *A.M.A. Arch. Dermat.*, 77: 122-123,1958.

*Zephiran®, Winthrop Laboratories, New York.

FOR LOCAL ANESTHESIA, A SIMPLIER METHOD

An even simpler method for producing local anesthesia is the intradermal injection of 1 to 3 cc. of sterile, isotonic, saline solution which will produce an elevated wheal, with pallor, which is completely anesthetic for 10-15 minutes.[5] This is particularly valuable for those in whom procaine or allied drugs produce untoward reactions. Because of its safety and cheapness, this technique deserves wide usage for minor skin surgery.◀

5. Shelton, J. M., *A.M.A. Arch. Dermat.*, 75:130, 1957.

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Prolonged or excessive menstrual flow of functional origin can be treated both therapeutically and prophylactically with Enovid.

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She is again treated with similar doses from day 5 to day 25 for two or three additional consecutive cycles.

ORIGINAL ARTICLE

Management of Urinary Tract Infections in Obstetric Patients

Discussion of recent advances in the prevention, diagnosis and treatment of urinary tract infections in obstetric patients

ROBERT E. L. NESBITT, JR., M.D.,* *Albany, New York*

The incidence of urinary tract infections is second only to infections of the respiratory tract, despite the fact that the normal bladder is very resistant to infection.[1] Cystitis is due not only to the presence of bacteriuria, but also to stagnant urine or bladder trauma. Certain physiologic and anatomic alterations of the urinary tract during pregnancy and the puerperium predispose to stasis or partial retention of urine, as well as stretching and traumatization of the bladder. Also, in view of the high incidence of bacteriuria—as high as 11 per cent in antepartum and 70 per cent in postpartum women—it is surprising that only three per cent of pregnant women develop cystitis, and that only two per cent of all patients have pyelonephritis as a complication during pregnancy or the puerperium. Cystoscopic examination soon after delivery may show marked edema, hyperemia, and even submucosal hemorrhage. Vesical hypotonia tends to induce overdistension. Incomplete emptying with the accompanying trauma and the presence of bacteria produce optimal conditions for the development of infection. Analgesia and systemic anesthesia contribute to urin-

*Albany Medical College of Union University and Albany Hospital.

1. Marple, C. D., *Ann. Int. Med.*, 14:2220,1941.

ary stasis by disturbing proper bladder function during labor and the early puerperium.

Once clinical suspicion is aroused by a careful history and physical examination, the presence of urinary tract infection is confirmed by examining a catheterized urine specimen. When the rate of urine flow is rapid, the numbers of bacteria discharged in the urine may be small, the urine in the bladder may not have pooled for a long enough time to permit multiplication to significant levels. It is for this reason that the first morning specimen is preferable. Also, certain organisms grow poorly in urine and pH and dilution may limit bacterial multiplication.

Even carefully collected specimens may be accidentally contaminated, since the catheter must pass through the meatus and urethra. However, accidental contamination of a fresh specimen will be too slight to be significant. For practical purposes the Gram stain of the freshly collected urine will differentiate contamination from infection, since organisms are readily found in stained specimens of urine when the high counts are present.

MANY CHRONIC INFECTIONS SYMPTOMLESS

Chronic infection may exist without symptoms or signs, or even obvious pyuria, thus it is important to recognize the chronic and insidious nature of certain cases of urinary tract infection. When these patients are neglected or overlooked, extensive upper tract involvement may develop with persistent hydro-ureter and hydro-nephrosis for weeks or months. The possibility of such involvement must be thought of when dysuria, frequency, and urgency are listed as symptoms, for they are more common in pyelonephritis than are flank pain, fever, chills and other generalized evidence of sepsis.

COMMON ORGANISMS

Although Escherichia Coli and closely related organisms are the most commonly found bacteria in most series of acute urinary infections, the relative percentage of staphylococci, enterococci, and members of the genera Proteus, Aerobacter and Pseudomonas increase in the chronic and complicated infections, particularly those following instrumentation, catheterization or prior antibacterial therapy. Acute uncomplicated infections are usually caused by a single organism, whereas the incidence of pure cultures may be as low as 20 per cent in infections complicated by structural abnormalities of the urinary tract. It is important to determine the type or types of bacteria involved by obtaining a culture of the urine prior to the institution of therapy. The effectiveness of therapy depends largely upon the sensitivity of the pathogens involved to the therapeutic agents in effective concentrations at the site where the bacteria occur.[2-4] Tests of sensitivity are mandatory in cases which have failed to respond to medication.[5] Since chronicity of infection and structural abnormalities go hand-in-hand, still more elaborate procedures such as kidney function tests, cystoscopy (with differential cultures from both ureters) and retrograde pyelography, are justifiable in refractory cases. Unless the need is urgent, these studies are best

2. Giertz, G., & Gulbring, B., *Acta chir. scandinav.*, 102:121,1951.
3. Högman, C., & Tillegard, P. A., *Acta chir. scandinav.*, 107:282,1954.
4. Jönsson, G., & Erlanson, P., *Acta chir. scandinav.*, 107:1,1954.
5. Möller, O., & Wenckert, A., *Acta chir. scandinav.*, 101:396,1951.

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A single short course of injections—1 ml. daily for 6-8 days—provides prompt relief which persists for months in most patients, and can be maintained by occasional booster doses.

Anergex therapy suppresses allergic manifestations, regardless of the offending allergen, thus eliminating skin tests, special diets, and long drawn-out desensitization procedures.

Over 500 documentated case reports[1,2,3,4,5] show that Anergex provided marked improvement or complete relief in over 60 per cent.

Anergex is effective in: seasonal and nonseasonal rhinitis (pollens, dust, dander, molds, foods); allergic asthma; asthmatic bronchitis and eczema in children; food sensitivities.

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reprints and literature available *Reg. U. S. Pat. Off.

1. Clin. Med. 2:1009, 1955.
2. Amer. Pract. & Digest Treat. 9:1447, 1956.
3. Clin. Med. 3:1059, 1956.
4. Amer. Pract. & Digest Treat. In press.
5. Files, Medical Department, Mulford Colloid Laboratories.

deferred until the postpartum period, because of the hazards of irradiation upon the fetus. Constant drainage of the bladder and catheterization of the ureters are rarely indicated during pregnancy.

SULFONAMIDES

The value of sulfonamides in the treatment of urinary tract infections is well established. In recent years, *Gantrisin* has gained in popularity and is gradually replacing sulfadiazine. Mixtures of sulfonamides have theoretical advantages in terms of solubility in urine, but these mixtures are not entirely free of reactions. In some instances, mixtures may be less effective than one of the component drugs alone.[6]

In most cases of acute infection the therapy is straightforward.[7-8] *Gantrisin* is effective against a wide variety of organisms, has few unpleasant side effects, and it costs much less than antibiotics. The usually employed dosage is 2 gm., orally, three or four times daily for a week to 10 days. The practice of frequent examination of the urine and blood of all patients receiving sulfonamide therapy is not as essential now as it was in previous years. Nissen and co-workers[9] have determined that the renal toxicity of several of the commonly used sulfonamides is about the same, and that the incidence of hematuria is about 2.0 per cent. Additional measures include a large fluid intake and appropriate bed rest. At the end of therapy, a catheterized urine specimen should be obtained for microscopic and bacteriologic studies.

6. Kimmelman, L. J., et al., *J. Urol.*, 65:668,1951.
7. Rhoads, P. S., et al., *J.A.M.A.*, 148:165,1952.
8. Stenderup, A., et al., *Acta med. scandinav.*, 144: 124,1952.
9. Nissen, N. I., et al., *Acta med. scandinav.*, 138: 301,1950.

NITROFURANTOIN

Nitrofurantoin is an effective orally administered antibacterial chemotherapeutic agent which presents no problem of crystalluria. Experience has demonstrated its value against certain sulfonamide-resistant organisms. Furthermore, these studies indicate that microorganisms, *in vitro* and *in vivo*, appear not to develop resistance to Nitrofurantoin. Both gram-positive and gram-negative organisms are sensitive, including many strains of such refractory species as Aerobacter, Psuedomonas, and Proteus species. The usually employed dosage of 50 to 100 mg. four times daily has not produced significant toxic reactions. Best overall results in pregnant and puerperal patients are achieved in patients treated with 100 mg. four times daily.[10] Smaller doses may suffice occasionally or as prophylaxis against acute exacerbation during pregnancy in patients with a history of recurrent infections.

ANTIBIOTICS

It would seem wise to choose one of the commonly used drugs with a long and proved history of clinical use and effectiveness, and to learn to use it well. Antibiotics should be reserved for the more complicated and serious infections, particularly those resistant to sulfonamides, and selected in accordance with the sensitivity tests on the organisms.[11] Relapses and treatment failure in the acute complicated cases may number up to 20 per cent of the total treated group. Penicillin is likely to be effective in staphylococcal infection in patients with no recent hospitalization, in-

10. Nesbitt, R. E. L., Jr., & Young, J. E., *Obst. & Gynec.*, 10:89,1957.
11. Kass, E. H., *Am. J. Med.*, 18:764,1955.

strumentation or penicillin therapy. This antibiotic is also effective in clearing many enterococcal infections of the urinary tract. Although Polymyxin B has a high incidence of renal and neurologic toxicity, it may be highly effective in certain resistant cases of E. coli, A. aerogenes and Ps. aeruginosa. The tetracycline group is especially active against E. coli, A. aerogenes, staphylococci and enterococci, although the individual drugs in this group may have significant differences in therapeutic results at times.[12-13] Erythromycin has an antibacterial spectrum similar to that of penicillin. Streptomycin is occasionally of value in the treatment of refractory infections when cultures have been repeatedly negative for acid-fast organisms. It should be borne in mind, however, that the capacity of streptomycin to induce drug resistance is probably greater than of any other commonly used antibiotic.[14] Some cases are probably better treated with multiple drugs. Although the advantage is not great and combination of drugs occasionally are mutually inhibitory, they may be additive or synergistic in some cases.[15]

INTRAVENOUS USE

Certain antibiotics may be administered by vein, such as terramycin or aureomycin, whereby 250 mg. of drug is mixed with 500 ml. of glucose solution, and administered over a four hour period. This may be repeated every four to six hours and has an additional advantage of ensuring adequate fluid intake, for patients unable to retain fluid by mouth. The clinical response to antibiotic therapy has not been very favorable, because the control rate in chronic and complicated infections, the group of cases in which these agents are chiefly used, is lower than in acute, uncomplicated infections.

A patient is classified as "cured" when she is asymptomatic and cultures of the urine are negative following treatment. The obstetrician has not discharged his responsibilities until the urine is proved free of offending organisms by repeated cultures. Eradication of drug-sensitive bacteria is possible in more than 90 per cent of the cases. When re-infection occurs, it is most often due to bacterial strains different from those originally present, although it may be of the same species. Inadequate treatment during pregnancy may lead to recurrence of acute symptoms or harboring of infection for months or years following delivery. Some may have extensive fibrosis of the ureter, others may harbor a smoldering, chronic pyelonephritis with deficient renal function. Chronic pyelonephritis is a more frequent cause of Bright's disease than is chronic glomerulonephritis, and is the most common renal lesion in uremia.[16] Some of these patients with hypertension, albuminuria and edema may simulate toxemia of pregnancy closely, and may receive inadequate and inappropriate therapy for their disease.

Some of the older methods of treatment of urinary infections, such as mandelic acid and methenamine mandelate, when used properly, are effective in most acute uncomplicated infections, and helpful for relief in otherwise intractable infections.[17] It is

12. Blahey, P. R., *Canad. M.A.J.*, 66:151,1952.
13. Womack, C. R., et al., *Arch. Int. Med.*, 89:242, 1952.
14. Wright, S. S., et al., *J. Lab. & Clin. Med.*, 42:877,1953.
15. Hobby, G. L., Ed. by H. Welch, Medical Encyclopedia, Inc., pp. 263-288,1954.
16. Jackson, G. G., et al., *M. Clin. North America*, 39:297,1955.
17. Knight, V., et al., *Antibiotics & Chemother.*, 2:615,1952.

imperative, however, that these patients be adequately investigated to rule out structural defects. Bladder tumors may manifest themselves as chronic cystitis for weeks or months before the nature of the lesion is suspected.

Every effort should be made to prevent the occurrence of acute urinary tract infections in pregnant patients, especially those who have had recurrent or chronic infections. Meticulous prenatal care, attention to the bowel habits, prophylactic drugs as indicated, frequent urinalyses, and instruction in the early symptoms and dangers of urinary infection will do much to lessen the risk of acute or subacute exacerbations.

The possibility of serious effects of urinary infections, on mother and fetus, demands early diagnosis and treatment. If the patient has fever, chills, nausea, vomiting, oliguria, acidosis, or "toxic" reaction, hospitalization and careful management is imperative. Thorough investigation, hydration, bacteriologic and hematologic studies, and good nursing care require hospital facilities. It is vitally important to surround these patients with proper safeguards if immediate and delayed maternal morbidity is to be minimized and maximum fetal salvage is to be effected.◀

Cutaneous Manifestations of Systemic Disease

Skin lesions may be caused by a variety of stimuli. Since these same factors cause systemic disease, it should follow that cutaneous manifestations of systemic disease will be evident if we search for them, but are likely to be missed if our index of suspicion is low.

The following listing of systemic diseases which may be manifested by cutaneous lesions may be helpful:

Congenital: Hereditary hemorrhagic telangiectasis, Von Recklinghausen's disease, adenoma sebaceum, Werner's syndrome.

Metabolic: Pseudoxanthoma elasticum, necrobiosis lipoidica, hemochromatosis, nevus araneus, gouty tophi, xanthoma, Leiner's disease, functioning carcinoid.

Avitaminoses: Follicular hyperkeratosis, angular stomatitis, Sjogren's syndrome, pellagra.

Malignant: Hodgkin's disease, leukemia cutis, lymphosarcoma, metastases, mycosis fungoides.

Microorganisms: Tuberculosis, tularemia, syphilis, typhus, Rocky Mountain spotted fever, the systemic mycoses, exfoliative dermatitis of Ritter.

Endocrine: Keratoderma climactericum, acanthosis nigricans, diffuse scleroderma, Addison's disease, dermatomyositis, myxedema.

Toxic: Disseminated lupus erythematosus, erythema multiforme, erythema nodosum, toxic erythema, leukemids, pustular bacterid of the palms and soles.

Allergic: Atopic dermatitis, urticaria.

Psychic: Delusions of parasitosis, neurotic excoriations, feigned eruption.

Thompson, R. C., *J. Tennessee M.A.*, 51:173-177, 1958.

ORIGINAL ARTICLE

Choosing A Diuretic

The choice of a diuretic must be based upon the etiology of the disease entity causing edema

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Choice of a diuretic varies with the condition causing the fluid retention. Correction of the basic disorder in beri-beri or thyroid disease may effect all the diuresis necessary. There is no universal diuretic (that is, one useful in every situation) and such a search is not even feasible. Therefore we must choose the diuretic drug for the particular condition to be treated with as much specificity as is possible in our present state of knowledge.

So many modifications of older drugs and so many completely new chemicals have appeared in recent years, that it is almost impossible for any doctor to be fully informed in this therapeutic field. To be kept in mind are the virtues of the common valuable measures, such as diet, rest and digitalis.

ORGANOMERCURIAL COMPOUNDS

These drugs act by depressing tubular reabsorption of sodium, chloride and water. Meralluride[1] is the most extensively tried and tested of the diuretic compounds. Therefore, all other diuretics are best evaluated by comparison with this drug. No oral mercurial preparation is as potent or dependable as those for parenteral use, and all cause gastrointestinal irritation in a large percentage of patients. Chlormerodin[2] is the most effective drug in this group.

1. *Mercuhydrin®*, Lakeside Laboratories, Milwaukee, Wisconsin.
2. *Neohydrin®*, Lakeside Laboratories, Milwaukee, Wisconsin.

The chief contraindication to mercurial diuretics is renal impairment. If albuminuria, with or without nitrogen retention, is a by product of heart failure, these drugs may be used, to be discontinued if diuresis is not obtained within several days.

Priming for three to five days prior to administering the parenteral mercurial with ammonium chloride, four to eight gm. a day, and acetazolamide[3] 250 mg. to 500 mg., twice a day may greatly enhance the diuretic action of the mercurial. Treatment of the edematous individual for the first time should begin with .5 cc. to 1.0 cc. of the mercurial diuretic. The majority of patients in need of a constant diuretic regimen are maintained on 1 cc. to 2 cc. dosages, on a weekly or biweekly schedule. If there is less than a two-pound weight loss in a 24-hour period following the injection of 2 cc. of the drug, the patient is either refractory to the medication and needs another diuretic, a different regimen of either reinforcement or substitution of the mercurial used, or the diagnosis of excess fluid retention is a mistaken one.

XANTHINES

Theophylline ethylenediamine (aminophylline) has been widely utilized for many years. Oral, rectal and parenteral routes of administration each have their advocates. Doses of 0.2 gm. four times a day are most commonly used. It is a mild diuretic by itself but its use in conjunction with the organomercurials may spell the difference between inadequate and adequate diuresis. Sensitivity to xanthine derivatives is manifested by headache, nervousness, nausea, vomiting, cramps and diarrhea. Convulsions may be precipitated in epileptics. Urticaria also occurs at times. Others of this group are theobromine calcium salicylate[4] in doses of 1.0 gm. four times a day, theobromine sodium acetate,[5] 0.5 gm. four times daily, and theophylline, 0.2 gm. four times daily.

AMMONIUM CHLORIDE

Ammonium chloride is an acid salt usually used in conjunction with the organomercurial diuretics to reinforce the action of the latter. It is especially useful in cases that have failed to respond to the mercurials due to the development of hypochloremic alkalosis. Metabolic and respiratory acidosis are a contraindication to its administration. Many patients experience gastrointestinal irritation from its use. It is best given in four to eight gm. dosage for several days prior to the administration of a parenteral mercurial compound. The enteric-coated preparations cause less gastrointestinal symptoms but are less efficacious, since many of the tablets pass unchanged through the intestinal tract.

CARBONIC ANHYDRASE INHIBITORS

Carbonic anhydrase is an enzyme that catalyzes the conversion of carbon dioxide and water to carbonic acid in the renal tubular cells. The breakdown of carbonic acid produces hydrogen ions, which are then available for replacement of the sodium ions in the tubular urine and also for the manufacture of ammonium ions. The inhibition of the action of carbonic anhydrase promotes diuresis by increasing sodium and potassium bicarbonate excretion in the urine and decreasing excretion of ammonium

5. *Diamox*,® Lederle Laboratories, Pearl River, N.Y.

4. *Theocalcin*®, Knoll Pharmaceutical Co., Orange, N.J.
5. *Thesodate*®, Brewer & Company, Inc., Worcester, Mass.

ions. With this loss of bicarbonate the urine becomes alkaline, plasma bicarbonate falls, and a metabolic acidosis develops. The sulfonamides demonstrate this diuretic effect. Acetazolamide is used in doses of 250 mg. to 500 mg twice a day intermittently so as to avoid the development of severe metabolic acidosis. It may be used to implement the mercurial parenteral diuretics or substitute for them advantageously in cases of cor pulmonale, in which its effect is most dramatic. Untoward effects that have been noted are agranulocytosis, thrombocytopenia, fever erythema, liver and renal lesions, paresthesias circumorally and in the extremities.[6] Clinical experiences with a new carbonic anhydrase inhibitor, p-sulfamyl-2 hydroxy-ethyl-carbanilate[7] which appears to be less toxic and more potent than acetazolamide were recently reported.[8] These drugs, though dangerous if used in too large dosages in Laennec's cirrhosis, at times cause a diuresis in cases recalcitrant to other diuretics. The carbonic anhydrase inhibitors, when used judiciously, have a definite place in the diuretic armamentarium, especially in cor pulmonale as a primer for the organomercurials and when used with great caution in Laennec's cirrhosis. Although these compounds are new, more is known of their physiologic actions than of even the tried and tested mercurials.

URACIL DERIVATIVES

Aminoisometradine[9] and aminometramide[10] effect diuresis by inhibiting tubular reabsorption of sodium. They are given orally and have few side effects. They are particularly effective in patients in the earlier phases of failure. Aminoisometradine is the more potent of the two drugs. Suggested dosage is 200 mg. twice a day.[11]

TRIAZINE

These compounds are derivatives of formoguanamine. Chlorazanil is given orally and its predominant effect is the augmentation of sodium and chloride excretion.[12] It is still too early to state their place among the diuretic agents available.

CATION EXCHANGE RESINS

Patients find this type of medication objectionable mainly due to its bulk. These resins act by removing sodium from the gastrointestinal contents. Potassium and calcium are also removed. Carbocrylamine[13] contains potassium so as to prevent the development of hypokalemia. The recommended dose is 15 gm., three times a day at meals. A contraindication to their use is renal insufficiency. The resins are most useful in Laennec's cirrhosis refractory to other diuretics.

HORMONES

The steroids have been widely used but at present the only definitive place they have found as a diuretic has been in the nephrotic syndrome. In edematous states due to cardiac failure and Laennec's cirrhosis they may be indicated when other diuretics have failed. Diuresis results at times either during or upon discontinuing therapy.

UREA

Urea acts by increasing glomerular filtration. The chief disadvantage of

6. Rubin, A. L., et al., *Ann. Int. Med.*, 42:258-368. 1955.
7. *Sulocarbilate®*, Warner-Chilcott Laboratories, Morris Plains, N.J.
8. Hirshleifer, I., et al., *New England J. Med.*, 257: 1074-1076,1957.
9. *Rolicton®*, G. D. Searle & Company, Skokie, Illinois.
10. *Mictine®*, G. D. Searle & Company, Skokie, Illinois.
11. Settel, E., *Postgrad. Med.*, 21:186-190,1957.
12. Ford, R. V., et al., *J.A.M.A.*, 166:129-136,1958.
13. *Carbo-Resin®*, Eli Lilly & Company, Indianapolis.

urea is its taste and odor. It may cause nausea, vomiting and diarrhea at times. It may be used with meralluride to potentiate its action. Its taste is best disguised by giving it in fruit juice or beer. It is utilized mainly as a last-resort diuretic. Dosage is from 45 to 90 gm. daily.

CHLOROTHIAZIDE

A comparison study of five oral diuretic agents concludes that chlorothiazide,[14] a sulfamyl compound, is of all orally administered drugs, the most potent for the therapy of all classes of edema.[12] While this is probably true it would be premature to dismiss the therapeutic effectiveness of the oral diuretics already described, for example, as reinforcement and priming agents for the mercurial diuretics, in intractable edema, and in cases in which a mild diuretic is all that is needed.

Although related chemically to the carbonic anhydrase inhibitor compounds, chlorothiazide has a different mode of action. How it increases sodium and chloride excretion is not known. The suggested dosage is 0.5 gm. to 1.0 gm. twice daily. Temporary refractoriness has been noted. The lassitude and lethargy complained of by many patients may be due to the hyponatremia produced by the drug.

CONCLUSION

Before choosing a diuretic one must first learn all he can about the etiology of the condition to be treated. Our primary concern is treating the disease, our secondary concern is ridding the body of retained excess water. We are fortunate to have many potent diuretics that act in various ways, to choose from.

Meralluride[1] is still the most potent and reliable diuretic we have at the present time and therefore is the clinical yardstick against which we can measure the therapeutic effectiveness of all other medications in this field.

Chlorothiazide[14] is the most overall potent orally administered diuretic.

More is known of the mode of action of the carbonic anhydrase inhibitors than of any of the other diuretics, and Acetazolamide[3] is an excellent drug for use in cor pulmonale.

The Xanthine derivatives, while weak diuretics, may be used to implement the more potent ones.

Ammonium chloride may spell the difference between lack of response and good diuretic effectiveness of the mercurials.

Aminoisometradine[9] is a diuretic that works well in mild cases of cardiac failure.

The triazines are still in the experimental stage.

The cation exchange resins may be useful in Laennec's cirrhosis, so recalcitrant to the action of other diuretics.

The steroids work well in the nephrotic syndrome and are to be tried in cases of fluid retention when other diuretics have failed. Urea may similarly be used as a last resort.

All these drugs have varying degrees of effectiveness and ranges of usefulness. Diet, rest, digitalis and its derivatives, mechanical removal of fluid by thoracentesis and paracentesis, phlebotomy, cardiac and abdominal-vessel surgery are methods not to be overlooked.

There is no panacea in the diuretic field, but with a good knowledge of drugs and methods available, the physician is able to do far more for his water-logged patient than ever before. Indeed, "dropsy" has now become a very manageable condition.◀

14. *Diuril®*, Merck Sharp & Dohme, Inc., Philadelphia.

Chemotherapeutic Agents

A discussion of the properties of some newer chemotherapeutic agents is presented in brief form

ALDONA BALTCH, M.D., *Syracuse, New York*

V Cillin K is slightly acted on by the gastric juice, hence is the best penicillin for oral administration. Taken before meals, it gives blood levels twice as high as those from penicillin V (8 mcg. per ml.) in 30 minutes. If taken after meals, levels similar to those of penicillin V (4 mcg. per ml.) are attained. At the end of two hours the two preparations produce similar blood levels (2 mcg. per ml.).

Kynex (sulfamethoxypyridazine) is a new sulfonamide with high plasma and urine solubility and low urinary excretion. Blood levels after a single dose are maintained for 48 hours and longer. The average dose is 1 gm. daily. It may cause systemic toxicity similar to other sulfonamides, but because of its high urine solubility hematuria and crystalluria occur rarely. Its distinct advantage is that daily dosage regimens are simpler than the more soluble sulfonamides because less is needed less often.

Vancomycin is a new antibiotic isolated from Streptomyces orientalis. It is active against Gram positive microorganisms (including penicillin-resistant staphylococci) and spirochetes. It must be given intravenously, after which 67 per cent may be recovered from the urine within 24 hours. Tissue concentrations and penetration into the cerebrospinal fluid and bile are poor. A cumulative action is noted if it is given more often than every eight to 12 hours. Bacterial resistance de-

velops slowly. The known important complications are local thrombophlebitis, occasional rash (4%), and chills. The average dose for therapy of a serious staphylococcal infection is 2 gm. daily given in two doses. Its main clinical usage is in the management of staphylococcal infections caused by organisms resistant to other commonly used antibiotics.

Oleandomycin (matromycin) derived from Streptomyces antibioticus is a white crystalline compound, soluble in water up to 5 per cent. It can be administered by both parenteral and oral routes. It appears to be effective principally against some Gram positive microorganisms, including the penicillin-resistant staphylococcus. Its toxicity is low. The chief disadvantages are that its therapeutic efficacy is one-third that of erythromycin, and cross-resistance develops with erythromycin and spiramycin. Thus, oleandomycin is of no value if the microorganism has become resistant to a superior drug, such as erythromycin.

This drug in combination with tetracycline is named *Sygnemycin*. The tetracycline effect apparently overshadows that of oleandomycin. Synergism between the two agents has not been proved.

Ristocetin (spontin) has been isolated in a crystalline state from a species of actinomycetes, Nocardia lurida. The drug is composed of two fractions, ristocetin A and B, the B fraction being three times more active antibacterially. Its activity is not significantly influenced by blood or serum. It is effective against Gram positive microorganisms, including penicillin-resistant staphylococcus. Its chief disadvantage is that it must be administered intravenously. Its use is followed by thrombophlebitis at the site of administration, occasional diarrhea, skin rash, drug fever, and (rarely) leukocyte depression without total bone marrow depression. Its activity is probably less than that of vancomycin in staphylococcal infections and should therefore be used when it and other agents fail.

Kanamycin, derived from Streptomyces kanamyceticus (Japan) is effective against tubercle bacilli, certain Gram negative organisms, and penicillin-resistant staphylococci. It is not very active against streptococci or pneumococci. It is given by the intramuscular route only. Penetration into the cerebrospinal fluid and muscle is poor. Fifty per cent of an injected dose is excreted in the urine in 24 hours. Toxicologic studies in humans are now in progress. Preliminary observations indicate that it may simulate streptomycin in its toxicity. With large doses albuminuria and casts occur, but no elevation of the nonprotein nitrogen has been noted. There is no cross-resistance between kanamycin and neomycin or streptomycin. Kanamycin may prove to be a valuable drug in management of infections caused by Escherichia coli, proteus species, Klebsiella, and penicillin-resistant staphylococci. Preliminary experiences suggest that in this last infection it may be the drug of choice.◀

New York J. Med., 58:2025-2026,1958.

Psychiatric Emergencies

Psychiatric emergencies ranging from the attempted suicide to the upset postpartum mother are discussed

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Early recognition and prompt treatment of psychiatric emergencies is the duty and privilege of general physicians.

Suicide must always be anticipated in depressed, delirious or acutely psychotic patients. To recognize these psychic disorders is to anticipate and prevent self-destruction. A depressed patient is apt to talk of suicide, of remorse, and say his family is better off without him. He is unable to plan for the future, is indecisive and feels lost. The neurotic with concurrent depressive anxious feelings uses the gesture of suicide to gain some point—either affection and solicitude, or, perhaps, the release of resentment held towards others. Such patients need not be put in a hospital, since having gained their point through threat or gesture they are for the time being satisfied.

A depressed, suicidal patient, however, should be put in a hospital and there every precaution taken against the possibility of self-destruction. Questions should be asked as to patient's thoughts of death, wish to live or die, ability to face and plan for the future.

ACUTE INTOXICATIONS

Acute intoxications including alcoholic, bromide and barbiturate overdosage are real threats to life. They may exist alone or in combination with any injury or illness in the

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- **CONFUSION**
- **APATHY**
- **ANTISOCIAL BEHAVIOR**
- **DEPRESSION**
- **LOSS OF MEMORY**
- **INABILITY TO CONCENTRATE**

NOTE: No side effects are observed save for occasional and transi
"niacin flush" in sensitive individuals.

1. Boernstein, W. S.: Tr. New York Acad. Sci. *20*:72, 1957.

ADDITIONAL REFERENCES: Smigel, J. O.: M. Tim
85:149, 1957; Levy, S.: J.A.M.A. *153*:1260, 1953; Thompson, L.
and Procter, R. C.: North Carolina M. J. *15*:596, 1954; Erv
H. J.: Missouri Med. *53*:1071, 1956.

REED & CARNRICK
Jersey City 6, New Jersey

ANALEPTONE ELIXIR
Each teaspoonful (4 cc) contains:
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Each tablet contains:
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Niacin ..... 50 mg.
Pepsin 1:10,000 ..... 5 mg.
SUPPLIED: Bottles of 100.

DOSAGE: One-half to one teaspoonful of Elixir; one to two tablets, 1 to 3 or 4 times daily.

course of which physical resistance is lowered. Such patients are best treated in a quiet, nonstimulating, restful, dimly lighted room with special nursing care. The presence of a few personal possessions such as photographs helps to keep the patient in close contact with reality. Adequate intake of fluids and maintenance of nutrition with small doses of insulin are in order. Reserpine intravenously is helpful. Restraints should be avoided whenever possible. Patients in delirium are frightened and must be protected against their own fears and prevented from panic reaction which may result in suicidal attempts to escape their projected fears.

ORGANIC MENTAL SYNDROMES

The psychic afflictions of senescence are frequently psychiatric emergencies. Keeping the patient in the familiar surroundings of home, limiting the number of visitors, giving special solicitous nursing care (best by a favored member of the family) and continued care by the physician are essential.

Help the patient to accept himself; show sympathetic interest in him as a person. Keep him in his own home, keep his life orderly and routine and free of nagging relatives. A night light should be kept burning to avoid fright, every new procedure should be explained beforehand.

ACUTE FUNCTIONAL SYNDROME

Fear of loss of control of thought and behavior may lead to desocialization, withdrawal, alienation from others, uncontrolled excitement or extreme inhibition. In the paranoid schizophrenic and manic-depressive reactions, the patient may have negative, hostile, destructive feelings toward persons on whom he is dependent. The conflict may erupt in violent, uncontrolled, aggressive behavior, often preceded by physical complaints of vague, often bizarre nature for which the patient will accept no reassurance or explanation. Expressions of hatred and of obviously false beliefs are diagnostic. When the hatred becomes so intense that the patient can no longer contain himself, he will project his feelings of hostility upon others, feel in danger of attack and therefore attack others or himself. The warning signs are increasing tension, increasing agitation, resentment and demands on others. Putting the patient in a hospital and the administration of promazine are essential.

Paranoid reactions in post-surgical patients, which occur frequently, are best treated with frank discussion of misinterpretations and misidentifications, and with assurance and orientation to reality.

ANXIETY STATES

The acute anxiety attack is usually related to aggressive thoughts and fantasies which are very frightening to the patient. These states are frequently precipitated by visual scenes of violence on television or motion picture programs. The patient feels his heart palpitating, has difficulty in breathing, is sweating or feels chilly, and there is a great fear of impending death. Sleep produces disturbing dreams in which he relives threats of his childhood. He wants to call for help but is unable to speak.

Any semblance of aggression in the treatment—force, restraints, hustling or mishandling of the patient—is contraindicated, but a firm, kindly and authoritative touch will be of immeasurable help.

Here reassurance, adequate sedation, the use of a motherly nurse and temporary relief from maternal responsibility will often lessen the intense agitation. Feelings of inadequacy and fears of hurting her child may develop after the patient leaves the hospital, particularly in the neurotic anxious patient. The most effective treatment is sedation and psychotherapy.

California Med., 88:347-349,1958.

Treatment of Depressive States in a General Hospital

Reactive depression must be differentiated from psychotic depression. In both the reactive and endogenous depressive states, insight is preserved and the ego, although disturbed, seeks restoration and recovery. Treatment of choice for the former is psychotherapy. For psychotic depressions, psychotherapy is usually contraindicated.

Twenty five depressed patients were admitted to a general hospital over a period of 18 months. No special section of the hospital was set aside, and no specialized nursing care was available. The patient was accepted only if he and his family were willing to accept responsibility and to cooperate. The longest period of hospitalization was 21 days, the shortest seven days. The patients were 20 to 76 years of age, 10 were men, 15 women. Seven were schizophrenics with depression which covered delusional and hallucinatory states who, after four to eight treatments, had to be transferred to various mental hospitals. Four were psychoneurotics who responded quickly to psychotherapy and mild sedation. The remaining 14 were either of the manic-depressive, depressed type, or involutional depressives. All in this group responded to treatment. Five returned within a month or two for another series, and several had to receive a third series.

Two patients had hypertension and myocardial damage and were treated with convulsive therapy with good results. One case of lymphatic leukemia, accidentally discovered, responded to four treatments and was referred to a hematologist.

In most cases there was a marked improvement after the second or third treatment. Another three or four convulsive treatments were usually given to insure stability. Most recovered patients refused to stay longer than two or three days following their last treatment. Severe post-shock confusion sometimes occurred when treatment was given daily. In those who received the standard three treatments weekly, no significant confusion occurred.

Intravenous barbiturates were carefully avoided. Succinylcholine chloride, 10 to 15 mg., was given intravenously immediately prior to treatment to prevent too-violent convulsions. Meprobamate, 400 mg. orally, and atropine sulfate 0.6 mg., intramuscularly, were given ½ hour prior to treatment. Following the convulsion, a few whiffs of oxygen were administered and the patient was placed in restraints for 30 minutes to prevent falling out of bed or annoying others during the post-shock confused state.

Weber, J. E., *Wisconsin M.J.*, 57:200-202,1958.

Physiological Measurements of "Emotional Tension"

Electroencephalographic, respiratory, vasomotor and dermo-electrical changes were recorded in an effort to determine the changes during tension

BRIAN ACKNER, M.D., and G. PAMPIGLIONE, M.D.,
London, England

There is no such thing as emotion; it is an abstraction derived from certain subjective mental states and associated behavior and body changes. We talk about anxiety causing bodily changes, anxiety bringing on an attack of migraine and so on. Emotional states should be regarded as subjective epiphenomena which may occur concomitantly with bodily changes as accompaniments of stressful adaptations.

If both the subjective states and the observable changes arise from a common cause, it could be hoped that a full knowledge of one would provide us with some understanding of the other two. However, we do not even know to what extent the various bodily changes are intercorrelated, nor can we quantify "emotional stress," which is dependent on factors both without and within the individual. We can expose subjects to comparable stimuli or environmental factors, but it is the significance of the latter to the individual which determines whether at any particular time they will be stressful or not.

It is commonly believed that emotion causes visceral symptoms and influences the manifestations and course

of disease. A few hundred years ago emotion, the spring of action and conduct, used to sit in the heart, or in the belly, according to either Racine or Rabelais. Today emotion is considered an agitation of the mind, somehow involving the brain.

Several studies made by physiologists on bodily changes in emotion showed that there is no rigid parallelism between the occurrence and degree of agitation of the mind that the subject shows or experiences, and the occurrence and degree of measurable changes in the body.

In measurements of electroencephalographic, respiratory, vasomotor, and dermo-electrical changes, the variability in patterns from one subject to another was very marked and often difficult to predict. There were common trends and marked individual differences, but these did not appear to be clearly related to particular clinical features. Further, in some investigations the physiological changes revealed no gross differences between patients and members of the staff.

Previous work had shown that the administration of barbiturates in man may evoke fairly constant and therefore predictable changes in the activity of the brain as measured electrically, particularly in the frontal regions. When barbiturates are slowly injected into a vein a number of clinically observable changes may follow, such as drowsiness, difficulty in articulation, appearance of nystagmus, diminution in the speed and accuracy of movements, and sleep. In normal subjects as well as in patients no close correlation has been found between the beginning of any of these phenomena and the development of the EEG changes in response to the drug. Another investigation failed to establish any clear relationship between the time of appearance of the fast activity in the EEG and motor relaxation as recorded by a diminution in the action potentials from the muscles of the forehead and neck.

In the present investigation, it was found that some patients were more apprehensive than others about the test, and that the intravenous injection could not be carried out in several patients who either had inaccessible veins all the time, or marked venous constriction at the time of the test. Some patients were very restless with their arms and hands, increasing the difficulties of intravenous injection and of obtaining a reliable trace of the pulse volume waves from the finger. The sedation threshold is based on the combined occurrence of two phenomena: A change in speech (slur) and a change in the EEG. The injection was continued until the patient became unresponsive.

In view of previous experience patients suspected of cerebrovascular disease or other organic cerebral lesions were excluded from our series as their EEG response to barbiturates may be even more variable.

The point at which the gradient changes is called the "inflexion" point, and it has been demonstrated that the patient slurs within 80 seconds from this point. This combination of events determines the "sedation threshold."

It was found that although some of the curves obtained were S-shaped and slurring occurred near enough to the first inflexion, most of the other curves were complex with several inflexion points. In a few others the growth was slow but steady, without definite inflexions until the patient was asleep. Because of these various

difficulties a definite sedation threshold could be determined in only a third of the cases. This determination was impossible in another third of the cases and appeared doubtful in the remaining third.

The patients were divided into three groups according to the severity of their anxiety. There was no substantial difference in these three groups of patients in the amount of drug injected by the time the patient began to slur, and the mean amount of drug necessary to render the patient verbally unresponsive was remarkably similar in each of the three groups. The amount of drug necessary to reach the maximum amplitude of induced fast activity was also similar.

In order to assess the relationship between the "sedation threshold" and the diagnostic categories, our patients were grouped as follows:

1. Anxiety and neurotic depression.
2. Obsessional states.
3. Mixed neuroses.
4. Endogenous depressions.
5. Hysteria.

The mean "sedation threshold" was found to be the same (6 mg./Kg. body weight) both for the group of anxiety and neurotic depression patients and for the group of hysteria patients. The amount of drug required to induce responsiveness was not substantially different for each of these diagnostic categories. There was no correlation between the sedation threshold and the time and amount of increase in the pulse volume waves in these groups, nor any constant correlation with the variations in pulse-rate.

When the injection of sodium amytal is continued at the same rate until the patient becomes unresponsive, a single clear inflexion point in the curve of induced fast activity in the EEG is recognizable only in a limited number of cases. The slur therefore should be essential in deciding which of a number of inflexion points is to be used in determining the threshold.

It seems likely that a subjective judgment of "slurring" could unconsciously be influenced by a knowledge of the patient's emotional state (or diagnostic category) with the production of correlations not obtainable by more objective methods of investigation.◀

Proc. Roy. Soc. Med., 51:76-81,1958.

Causes of Death Among Adolescents

In this country cardiovascular and renal disease and malignant neoplasms each account for 10 per cent of the deaths of patients between 10 and 19 years of age. Accidents are the main cause of death for this age group: they cause 55.1 per cent of deaths at ages 15 to 19—the male-to-female ratio is 3:1.

For the group aged 15 to 19 in 1955, the death rate per 100,000 (regardless of sex) from all forms of tuberculosis was 0.9, from poliomyelitis 0.9, from neoplasm 7.9, from diabetes 0.1, from cardiovascular disease 6.1, from motor-vehicle accidents 34.5 (male 52.1, female 16.9), from all other accidents 18.2 (male 31.6, female 4.7) and from suicide 2.6.

Gallagher, J. R., et al., *New England J. Med.*, 259: 24-31,1958.

Causes and Evaluation of Chest Pains

The differential diagnosis of chest pain may depend upon the type of pain as well as upon the history

E. CHARLES SIENKNECHT, M.D., *Knoxville, Tennessee*

The first question that arises is whether the pain is "heart pain." The patient should be questioned as to location, radiation, intensity, quality, and duration; relation to body position, eating, swallowing, belching, bowel movements, or flatus; relation to physical activity, worry, anxiety, or anger. It is important to note whether local tenderness has been felt in the chest wall in the area of the pain. The presence or absence of a respiratory component of the pain is often diagnostic. Let the patient describe the sensation and, then in subsequent questions, use his own words. The constricting quality of angina pectoris may not be called pain by the patient. The finding of a hiatal hernia by x-ray is no proof that the patient's symptoms are due to this. An abnormal electrocardiogram may be entirely innocent.

EXAMINE

Examine from head to toe for any bit of evidence. Slight swelling or tenderness of one leg may point to pulmonary embolism as a cause of chest pain. Use compression of the thoracic cage anteroposteriorly and laterally, fist percussion of vertebrae, and pressure over various parts of the chest.

LABORATORY PROCEDURES

X-ray and fluoroscopic examination, the electrocardiogram, and the varied laboratory procedures are of-

ten a great help, but there is no alternative to the skillful interrogation of the patient for localizing causes of the pain.

Chest pain is to be considered cardiac in origin if it is induced by effort, located substernally, constrictive or oppressive in type, radiating into the left shoulder or arm, of short duration, or relieved by nitroglycerin. On the other hand, noncardiac origin is to be assumed if pain occurs at rest, is located in the left chest, is aching, does not radiate, is of long duration, and is not relieved by nitroglycerin. In a study of 100 cases of known cardiac pain and of known non-cardiac pain, exceptions to the specificity of each of the six criteria varied from 15 to 40%. When one or more of the characteristic cardiac or noncardiac pain features were found, a definite diagnosis could usually be made.

PAIN OF CARDIAC ORIGIN

Anginal pain is often described as a choking, burning, squeezing, or aching type of pain, or at times merely as "gas." The patient rarely makes any other complaint. The discomfort is usually caused by exertion, emotion or cold; it is not sharply localized, may radiate to neck, shoulder, or one or both arms, is relieved by rest and nitroglycerin. Physical examination and diagnostic tests are usually of no value. Exercise electrocardiograms are not infallible.

Myocardial infarction pain is similar in location, but lasts hours rather than minutes. It may range from a crushing or constricting pain, severe enough to cause shock, to vague discomfort. The onset is little related to effort, may occur when at rest or asleep. Signs may include pallor, cold sweat, rapid weak pulse, tachycardia or marked bradycardia, drop of blood pressure below its normal level, and later a friction rub. After 24 to 48 hours there is an increase of white blood cells, rise of sedimentation rate and serum transaminase level. Diagnostic ECG's may be obtainable shortly after the onset of the attack, or they may be delayed for days. Severe or prolonged chest pain should be considered as due to myocardial infarction until proven otherwise.

Pericarditis pain may be hard to diagnose from coronary pain. The friction rub is apt to be heard from the time of onset rather than 48 hours later as in myocardial infarction. Typical ECG findings of pericarditis to complete resolution in the benign course confirm the diagnosis. The pain lasts longer than in angina pectoris, and may be aggravated by deep breathing, coughing, swallowing, or changing body position.

Pain from elevated pulmonary artery pressure is usually precipitated by exertion or emotion, but unlike that of angina may occur at rest. It is often accentuated by respiration or accompanied by dyspnea. When brought on by exertion it is relieved by rest, not relieved by nitroglycerin, and is usually strikingly relieved by oxygen. Often there is cyanosis with the pain. The diagnosis of the underlying disease must be sought. The ECG will frequently show right ventricular hypertrophy.

Dissecting aneurysm produces pain similar to, even identical with, that of myocardial infarction. The pain varies in location with the site of the rent in the artery, in radiation with the direction of progress of the dissection. Subsequent obliterations of pulse, neurologic signs, and hematuria may

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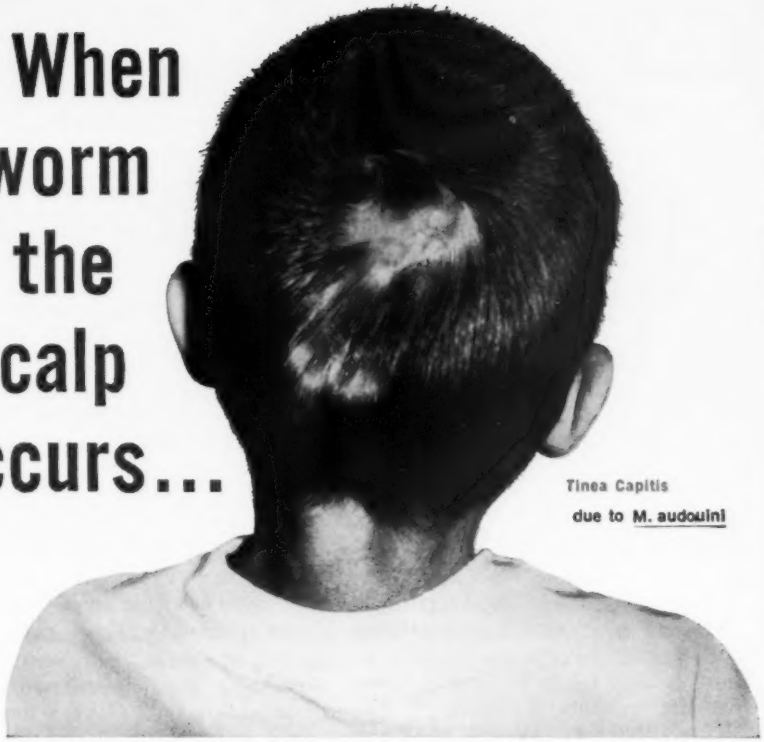

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or may not develop. The importance of making this diagnosis antemortem lies in the new achievements in surgical treatment which occasionally may permit the evacuation of the clot and the rechanneling of the dissection back into the normal aortic lumen.

Aortic aneurysm pain is boring or throbbing if from compression of adjacent structures, and particularly if sterum, ribs and vertebrae are eroded. Syphilitic aortitis produces a dull, continuous, substernal pain, which may be accentuated at night; it is not related to exertion. Diagnosis is readily made by use of x-rays.

The pains of neurocirculatory asthenia or effort syndrome and the hyperventilation syndrome are characterized by increased breathing over the actual need. The intercostal muscles may be tender during attacks, and the diaphragm, particularly on the left, may lag in its motion. Some patients mention tightness in the chest. Dizziness and light-headiness are usual, along with numbness and tingling of the face or extremities, tachycardia, and sighing. Twinges of pain may be felt in the left chest rather than substernally, following rather than during exertion. It is often possible to reproduce the symptoms by forced voluntary hyperventilation, and thus to confirm their origin.

PAIN OF NONCARDIAC ORIGIN

Pulmonary embolus is a common cause of chest pain which may be of pleuritic type or a severe precordial pain similar to that of coronary occlusion. A large embolus may produce shock similar to that of a myocardial infarction. Dyspnea and cough are common; hemoptysis following such a pain is diagnostic. A pleuritic type of pain should arouse suspicion of pulmonary embolism following injury, surgical operations, or childbirth. In cardiac conditions, particularly auricular fibrillation, it should be suspected.

Spontaneous pneumothorax may produce a pain similar to that of coronary thrombosis, even to radiating to the neck. Cyanosis and a rapid pulse may further confuse the picture. Physical findings should make the diagnosis obvious, and may be confirmed by x-ray findings.

Pain of esophageal origin is often confused with coronary pain. It has been variously described as burning, squeezing, pressing or aching, or as a feeling of fullness. It is usually substernal, may extend to neck, jaws, shoulders, arms, or back.

Pain due to hiatal hernia is accentuated by meals and recumbency. Dysphagia is common. The duration of pain is usually longer than that of coronary disease. Demonstration of a hiatal hernia does not assure that this is the cause of symptoms. We are often too eager to grasp the tangible finding of hiatal hernia rather than the important intangible history diagnosing angina pectoris.

OTHER DIFFERENTIAL DIAGNOSES

The difficulties in the differential diagnosis of gallbladder colic from basal myocardial infarction is notorious. A manifestation of the irritable colon syndrome, with trapping of air in the region of the splenic flexure of the colon, often produces a type of precordial pain radiating into the left pectoral area, the left side of the neck, the top of the shoulders, or the left arm. A carefully taken history easily detects the difference between angina pectoris and this condition which in-

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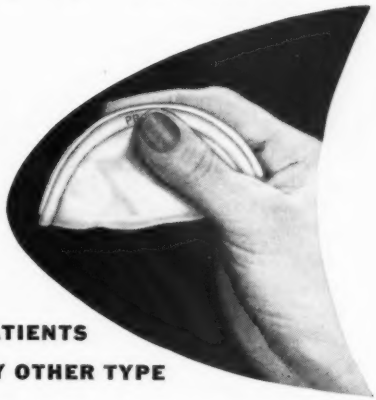

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FIG. 1.

FIG. 2

FIG. 3

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cludes gas, belching, bloating, or flatus, the passing of which often relieves the discomfort. Duodenal ulcer with perforation may cause severe, low substernal pain radiating to the shoulder, and a shock-like syndrome easily confused with myocardial infarction, as may acute pancreatitis.

Pain of the chest wall should be easy to diagnose, yet is often confused with cardiac pain and pain of other underlying structures. Tenderness of the chest wall and reproduction of the pain by pressure on the chest wall should differentiate most of these conditions.

Degenerative arthritis, protruded discs of the cervical spine, or tumors of the cervical spine may cause pain in the upper part of the chest, usually unilateral, and if on the left side may easily be confused with coronary pain. The pain is often aggravated by turning or hyperextending the neck, or by use of the upper extremities. The pain usually occurs at night and at rest.

SUMMARY

In an analysis of the histories of 100 patients referred for chest pain which was thought to be due to heart disease, only half were found to be due to definite heart disease; 44 per cent were associated with emotional difficulty and without definite organic disease. Pain located below the nipple, outside the nipples, or between the nipples and costal margin is rarely cardiac in origin. Momentary or sharp shooting pains are never so. Pain which varies in location, character or radiation is usually skeletal in origin. Chest tenderness over a prolonged period is not cardiac. Commonly, left arm pain is skeletal.

Because of the fear which it produces in the patient's mind concerning heart disease, cancer and tuberculosis, it is always imperative that sufficient time and effort be taken in the differential diagnosis of this symptom. Precise diagnosis is always greatly to be desired, and irreparable harm may be done following an unjustified diagnosis of heart disease. The value of a good history in this diagnosis can hardly be overemphasized.◀

J. Tennessee M.A., 51:269-275,1958.

Sudden and Unexplained Death in Children

When a child dies suddenly and unexpectedly, meticulous investigation of the cause should be mandatory

ISRAEL DIAMOND, M.D., *Louisville, Kentucky*

Cases of unexplained deaths in children are reported in the press at least a dozen times a year. The term, "sudden death" usually implies death occurring in an ostensibly healthy individual. Here it is unexpected death. In cases of children dying unexpectedly from natural causes, frequently recriminations occur in the family. Explanation of the cause based on sound investigation can usually prevent harm.

Some of the more frequent causes of such deaths are:

1. Poisons: Usually dramatic symptoms occur shortly after poisoning. It is discovered that poison has been taken, and a hurried trip is made to the doctor or emergency room. There are cases in which poisoning is either overlooked or remains undetected until death has occurred. Parents may have no knowledge of the child's ingestion of lead-containing substance. Lead poisoning may strike suddenly, with or without a convulsion, and coma progresses to death.

2. Foreign Bodies Ingested or Aspirated: A boy, two years of age, detached a colorless, plastic covering from the eye of a large panda doll. He got it into his pharynx, concave side forward. Two doctors inspected his throat with a flash light and failed to see the transparent object. It was detected at autopsy by the palpating finger.

Aspiration of gastric contents is dif-

ficult to interpret as a cause of death. Many infants, allegedly smothered, died of minor illness coupled with aspiration. Infants and small children sedated and fed by mouth are prone to this accident. Infants suffering from mild respiratory disease or diarrhea and those with more serious disease should be kept on the right side or prone.

In many instances the diagnosis of death by aspiration is made on too slight evidence. Many persons aspirate gastric contents in the agonal state. None of the findings, such as air block, atelectasis, or mucosal reddening is in itself evidence of significant aspiration. As a rule, however, agonal aspirates are slight in amount, do not occlude the airway and produce no significant changes in the lungs. The clinical data are of paramount importance.

3. Physical Agents Causing Traumas (electrocutions, strangulations and homicides): There is the occasional case of death resulting from trauma causing laceration of the spleen, lungs or aorta some hours afterward, leaving no external marks. A child's thorax may sustain sufficient trauma to rip a lung without any rib fractures, or even ecchymoses of the chest wall. Electrocution of crawling infants and toddlers is not rare and the proper protection of electrical outlets and grounding of electrical apparatus should concern every parent. There are occasional cases in which the evidence of electrocution may be easily overlooked.

It is possible for death by strangulation to occur rapidly, leaving no marks on the skin. Many infants and children are alleged to have been suffocated by bed clothes or by over-lying of the mother sleeping in the same bed. A few others are attributed to homicidal smothering using the hand or a pillow. Whenever a community has instituted confirmation of cause of death by autopsy, the incidence of these cases has dropped dramatically. Infants can give a surprisingly good account of themselves. It is possible for an infant to become asphyxiated by a loop of sheeting, or by getting its head through the bars of a crib. This is a rare occurrence, and infants thrive under layers of sheets and blankets. One child was strangled by the aperture of a zippered sleeping bag. Homicidal smothering may leave abrasions and scratches.

4. Infections: It is probably true that many cases attributed in the past to over-lying, smothering in the bed clothes, and status thymico-lymphaticus were cases of infection. The leading offenders are laryngo-tracheobronchitis and pneumonia. In the older children these are found along with other infections such as myocarditis, meningitis, encephalitis and peritonitis.

5. Congenital Anomalies: These may cause few or no symptoms until death occurs. Subarachnoid and intraventricular hemorrhage probably fall into this category. Congenital cardiac anomalies form the majority of these cases in childhood, particularly in infants. Some infants with badly damaged hearts make satisfactory progress until closure of the ductus arteriosus or a mild infection causes heart failure and unexpected death. Endocardial fibroelastosis is a notorious offender in this respect. This disease sometimes kills suddenly in the teens.

6. Blood Dyscrasias: The leading role is held by anemia. A negro boy, 4 years of age, dropped dead while play-

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ing in the yard. Autopsy revealed a striking fatty degeneration of the heart, an enlarged fatty liver and marked pallor of the organs. His hemoglobin was 4 gm. The cause of his anemia is not clear. The role of leukemia as a cause of sudden death is well established, as are the dyscrasias of coagulation.

7. Deficiency Diseases: Rickets and/or scurvy are well-known causes of sudden death in infancy. Recently two well infants, five and six months of age, died suddenly and showed gross edema of the heart consistent with the Beri-Beri heart.

8. Tumors: Tumors, especially brain tumors, can cause sudden death in a variety of ways. A slight hemorrhage within the tumor causes convulsions, coma, and death within a matter of hours.

9. Convulsions: In some children convulsions may cause a cerebral edema sufficient to cause death.

This by no means exhausts the possibilities. It does, however, provide a compelling list of reasons for adequate and detailed examination in these cases.

INVESTIGATION

There must be a competent post mortem examination. The circumstances attending the death and a detailed history of preceding events are of equal importance in the interpretation of the data. Even with optimal investigation by competent people, many cases of unexpected death remain unexplained.

The pathologist must not yield to the temptation of assigning a lesion as a cause of death merely because it is the only abnormality present. The solution of this problem will be furthered by a frank statement of, "I don't know." There is ample clinical and experimental evidence to indicate that death may occur through functional disturbance without morphologic change. The issues must not be obscured by misinterpreting the significance of low-grade or minimal pneumonitis, agonal aspirations of gastric contents and agonal congestions, hemorrhages and edema.

The diagnosis of status thymicolymphaticus should rarely, if ever, be made. It is preferable, in the absence of other facts, to consider such a death as unexplained rather than to attribute it to this cause.

SUMMARY

Sudden and unexpected death in infancy and childhood is a tragedy that requires meticulous investigation. Both society and the family benefit by the correct answer, and it will be obtained only through full autopsy investigation in which ill-founded notions and old wives' tales have no place. Some deaths, despite our best efforts, must remain unexplained in our present state of knowledge.◀

J. Kentucky M.A., 56:38-41,1958.

FINANCE

The Doctor Builds His Estate

Prepared for the readers of Clinical Medicine by the Research Department of the leading investment banking and brokerage firm of Bache & Co., 36 Wall Street, New York 5, New York

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These monthly articles point out one method by which the professional man may overcome the particular handicap imposed upon him by our tax structure, which taxes the bulk of his income at normal income tax rates, as opposed to the capital gains tax avenue open to many business men. One solution to this problem is the systematic investment of a portion of current income each year in securities. Such a program, which should include many different types of investments such as bonds, preferred stock, common shares and shares of mutual funds, will have as its objectives growth of principal together with reasonable income. We again emphasize that even the most complete series of articles of this type cannot take the place of consultation with a representative of a reputable brokerage firm.

Growth is probably the most misused word in financial circles. While almost everyone will speak well of it, there is no accepted definition of what really constitutes growth.

One school of thought looks primarily at a company's sales record. If sales advance steadily year after year, the company, to their way of thinking, is automatically a "growth company." The sales growth may have been accomplished through mergers with other firms that resulted in equity dilution that have kept earnings per share from growing, or the growth may have been accompanied by steady increases in costs that have kept earnings per share down, but the securities are called

growth stocks by this school.

We cannot agree with this approach, any more than we can go along with those who look only at the size of a company's assets, or the number of physical units of a company's product that are sold, the total earnings in dollars or number of offices or any other arbitrary measure. To us, a growth company is one in which earnings per share of common stock show a steady, substantial increase over the years. It is a certain number of shares of a company that the investor buys, not the whole company. An increase in total dollar earnings that is accomplished by the issuance of more stock to bring in the additional business and thus results in the same earnings per share doesn't help the individual stockholder at all.

With this thought in mind, we offer three stocks this month that, by our definition, are true growth stocks. Corn Products Company is a leading company in the food industry with a blue-chip reputation. Liberty Loan is a fast-growing small loan company. New Jersey Natural Gas Company is a lesser-known natural gas utility in the East, with a bright future and encouraging past record.

CORN PRODUCTS COMPANY

Corn Products Company, the entity resulting from the merger of Corn Products Refining Company and The Best Foods, Inc., appears attractive for long-term growth. While both firms in the past have been important in their own areas, the combination should lead to greater economies and to a much more dominant enterprise which will be in a position to more fully exploit the favorable opportunities in the food industry.

Contrary to expectations, food expenditures have risen steadily since the depression years of the 1930's, both in terms of dollars spent and as a percentage of total spending. Retail sales of food have continued to rise during the recent recession, a period in which personal income actually declined moderately.

This impressive record probably stems from a multitude of factors, but most of them are parts of the same overall trend—changes in the pattern of food consumption. These shifts include the growth of more expensive foods; improved techniques of freezing and pre-cooking which has shifted more and more of the preparation of food from the housewife to the food manufacturer; the spread of the supermarkets with their vast array of attractive items and impulse purchase stimulants; the rise of television viewing as a National pastime; the institutionalization of the coffee break, and the appearance of "gourmet" foods.

Moreover, with improved food processing techniques coming along constantly, we would expect these trends to continue. By 1965 the number of teenagers, our biggest eaters, will have increased by 40 per cent—triple the rate of expansion predicted for the entire population. In view of these facts, we think Corn Products Company will continue to prosper.

Both Corn Products Refining and Best Foods have excellent records in a competitive industry. The margins which these companies have been able to achieve have been better than most other companies in the industry. Best Foods has been a leading producer in its principal area. Its output includes such products as mayonnaise, other food items, shoe polish and allied products, as well as household fabric dyes. Its margarine division distributes its product under the trade name of "Nucoa" as well as "Holiday" at

lower prices. Other important products include "H-O" oatmeal and cream farina, "Presto" self-rising cake flour and "Skippy" peanut butter. The company's shoe polishes are retailed under the trade name of "Shinola."

Other food products include sliced fresh cucumber pickles and a blend of mustard and horseradish. The company refines and sells edible vegetable fats and oils to other companies. The household fabric dyes are made in a full line of colors and marketed under the trade name "Rit."

Best Foods has operated 10 plants in the United States and two in Canada. The company's products are being consistently supported by extensive advertising programs, both National and local, utilizing all basic media.

Corn Products Refining is a much larger company than Best Foods, and has a wider line of products. In the United States bulk products, which are sold to such customers as the baking, paper, confectionery, textile, canning, foundry, brewing and pharmaceutical industries, account for approximately 53 per cent of sales. By-products, account for about 32 per cent of sales, while consumer packaged products make up 15 per cent of the company's sales lines. About one-third of domestic sales are accounted for by non-corn derivatives.

The company's products include the famous "Karo" syrup, "Mazola" salad and cooking oils, "Kasco" dog foods, starches, puddings and "Bosco" chocolate milk amplifier.

As the largest manufacturer of corn-derived products in the U.S. and worldwide, Corn Products Refining has long been regarded as a firmly entrenched enterprise with a record of consistent earning power. From its inception it has been engaged in the wet milling of corn and the sale of starch, corn syrups and sugars, corn oil and animal feed ingredients. Based on these primary products, the company over the years has developed a variety of other industrial and household consumer lines.

Since the company's products have been fundamentally based on the use of corn as a raw material, the price of this commodity historically has been of vital importance to profit margins. Several acquisitions in recent years have been made in order to reduce this market dependence on corn prices, as well as to expand the overall operations at a more aggressive rate than has heretofore been demonstrated. The merger of Best Foods, of course, is a major step in this direction.

Corn Products operates 13 plants and owns or leases warehouses in 375 cities throughout the United States. The company's international subsidiaries own or lease plant sites, offices and warehouse space in many cities throughout the world. The international operations are of substantial importance, and were recently expanded through the purchase of a large German manufacturer of dehydrated foods and bouillon cubes. About one-third of the world-wide sales, and somewhat more of the earnings, of Corn Products Refining have been accounted for by its operations outside of the United States and Canada.

On a pro-forma basis—that is, using the 1957 year for Corn Products Refining and the fiscal year ended June 30, 1958, for Best Foods—sales for the combined companies totaled $450 million, with net income reaching $27.3 million, compared to $418 million in sales and net income of $26.3 million in the preceding year. Including the substantial foreign operations in the

Corn Products Company			
Price	46½	Capitalization	
Dividend	$2.00	Long-term Debt	$43,953,800
Yield	4.3%	Common Stock	10,814,518 shs
1958 Price Range	46½-33½		
Traded	N.Y.S.E.		

picture, these figures for the year would be $613.2 million and $31 million respectively, as compared with $526 million and $27.2 million in 1956. During 1957, domestic earnings came to $2.53 a share, compared to $2.48 in the preceding year. Including foreign earnings, the figures would be $2.87 and $2.56, respectively.

The steady growth inherent in this situation can be seen in the consolidated domestic and foreign earnings on a pro-forma basis for the new company for the last five years. Thus, over this period, earnings have risen from $2.18 a share in 1953 to $2.25 in 1954, and $2.45 in 1955, $2.56 in 1956 and $2.87 in 1957.

Perhaps the main strength of these companies, particularly Best Foods, has been in their very strong financial condition. In fact, each company appears to have excess working capital which can be used for internal expansion as well as acquisition of other companies. Both concerns have had a record of extending their product lines through favorable acquisitions. On a pro-forma basis, current assets as of June 30, 1958 approximated $122 million, including $35.6 million in cash and marketable securities. Current liabilities approached $40 million. Moreover, the relatively small amount of debt—$44 million—will permit the company to regularly expand through borrowing when favorable opportunities occur.

The dividend record of both companies is excellent. The shares for the new company will have an initial quarterly cash dividend of 50¢ paid in January.

In our opinion, the good quality shares of the merged company have appeal for conservative investors seeking a defensive security in a growth industry.

LIBERTY LOAN CORPORATION

Recent favorable acquisitions and rapid internal growth make Liberty Loan Corporation one of the fastest expanding major small loan companies in the industry. In 1954, a group of St. Louis businessmen acquired the controlling stock of this company. At that time, the small loan industry was expanding but Liberty was standing still, and in some cases going backwards. This trend has been rapidly reversed, and in the four years that the present management has been in control, expansion has been extremely rapid.

The principal business of Liberty Loan Corporation is the lending of small cash sums to individuals and families. However, many of the company's subsidiaries also engage in the sales finance business. The sales finance business, of course, consists of the purchase from the owners of installment notes arising from the retail sale of household furniture and appliances or other property and merchandise.

Some idea of the expansion of the company under the present management can be gleaned from the following figures: On June 30, 1954, the company had 66 branch offices. As of

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"daytime sedative" with less risk of accumulation or development of tolerance.

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year-end, 1957, 183 offices were in operation, and as of August 1, 1958, there were 229 branch offices. The company's notes receivable outstanding, which stood at $20.9 million in mid-1954 soared to $38.6 million at year-end 1957, and to $74.7 million on August 1, 1958. Total assets over this period rose from $24.4 million to $78.9 million.

In a finance company, of course, the number of branch office outlets has a very direct relationship to the total volume of loans made. In view of the fact that in a small loans operation most of the loans are made locally, a finance company has to reach a potential market through a great number of outlets. The present management of Liberty Loan has made considerable progress in this area, and future plans call for further expansion.

A good example of the methods that Liberty uses when moved into a new geographic territory was the extension of operations into California. On March 3, 1958, Liberty acquired two California companies with five branch offices. The company poured resources and personnel into the area so that 17 offices are now in operation in that area.

In the first eight months of 1958 alone, the company added 46 branch offices. Some 39 were acquired, eight were opened and one closed. The new states entered by the company in this period were California, Florida, Georgia, North Carolina, South Carolina and Texas. Five newly acquired offices were consolidated with existing offices. Liberty now operates offices in 176 cities and 25 states.

Volume of loans last year, including acquisitions, increased to $92.9 million from $70.3 million in 1956 and $35 million in 1954. This greater volume was the result of an increase in the number of customers served, which rose to 258,574 from 243,854 a year earlier and only 114,036 as recently as 1954. The average customer's loan also rose last year to $327 from $281 in the previous year. During the first six months of 1958, the company's volume of loans rose to $48.3 million from $40.4 million in the first half of 1957.

As of year-end 1957, notes receivable were $58.6 million, but "net" notes receivable, after deduction of $4.8 million of "unearned discount" and $1.6 million for "reserve for losses" were $52.2 million. This "unearned discount" is of paramount importance in estimating future earnings, since it is the reservoir of potential income. As loans outstanding are liquidated, this unearned discount will be transferred to the income account and should bolster future earnings considerably.

Last year, gross income increased 31 per cent to $12.1 million from $9.3 million in the previous year, and net income after taxes increased 16 per cent to $1.4 million from $1.2 million. Earnings came to $2.02 a share on the 629,929 shares of stock outstanding, as compared with $2.00 on a lesser number of shares existing at that time. In the first half of 1958, earnings rose again, to $1.07 a share from $1.01 a share in the first half of last year. As recently as 1954, full year earnings were $1.03.

The slight decline in profit margins last year—to 11.65 per cent of gross income from 13.12 per cent in 1956—was due primarily to larger provisions for losses, which climbed 62 per cent to $1.2 million, as well as to higher interest expenses. Interest ex-

Liberty Loan Corporation			
Price	39¾	Capitalization (6/30/58)	
Dividend	$1.50	Long-term Debt	$18,800,000
Yield	3.8%	Preferred Stock ($25 par)	160,000 sh.
Traded	O.T.C.	Common Stock	676,162 sh.

pense is a major factor in Liberty Loan's operations. Changes in interest rates play a significant role in profit margins from the overall earnings level. For example, in 1957 Liberty Loan had interest costs of $1.8 million, up $523,000 from the year earlier level.

Of course, part of the increase in costs can be attributed to the rise in total debt, which climbed to $46.1 million from the $36.3 million of the year earlier. Nevertheless, higher interest rates last year played a major role in the increased costs. When interest expenses are measured against the pre-tax net income of $2.5 million, it is clearly evident what impact changes can have on profit margins.

This year not only is the company experiencing lower interest rates, but it is also receiving the "prime rate" which it was not receiving last year. These two factors should expand profit margins considerably. Furthermore, the company's distribution of debt is favorable, and it is in an advantageous position to benefit from the lower interest rates. Of course, with rates now headed higher once again, this factor will prove of lesser importance.

Of total debt, short-term borrowings (principally bank loans) account for $26.7 million, long-term senior debt $8.6 million and subordinate debt $10.7 million. The exceptionally large percentage (58 per cent) of short-term borrowings is the portion that responds rapidly to changes in interest rates. This means that the company should see the benefits in its income account much sooner than most other companies in the industry.

At some future date, a rapidly expanding company like Liberty Loan would probably convert short-term bank loans into low-cost fixed senior debt. At the present time, however, there is no urgency to do so. Liberty Loan maintains unsecured credit lines with a large number of banks for approximately $41 million. In view of the fact that the company is now using only about $24 million, management feels that bank borrowings could very well be increased another $10 to $11 million before any such action need be taken.

The shares at current levels are selling at less than 20 times 1957 earnings, and less than 16 times 1958 earnings. While Liberty's price-earnings ratio is above the industry average, a number of factors, in our opinion, make the stock attractive for investors interested in long-term growth and capital gains.

NEW JERSEY NATURAL GAS COMPANY

Although at its present price we consider New Jersey Natural Gas Company stock rather fully valued from a defensive standpoint, we believe that the company has considerable further growth potential and that this potential, in time, should support higher values for the shares. The company has a distinctly capable management and serves a territory that is experiencing a high rate of economic development. Despite the sharp advance of the shares from a low of $19

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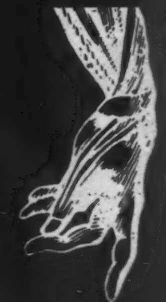

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Robins

remarl ably efficient skeletal muscle relaxant, ue in ch mical formulation, and outstanding for ined ac ion and relative freedom from adverse effects.

...ED REFEREN ES: 1. Carpenter, E. B.: Southern Medical Journal 51:627, 1958. ...h, H. F.: J.A M.A. 167:163, 1958. 3. Little, J. M., and Truitt, E. B., Jr.: J. Pharm. Therap. 119 61, 1957. 4. Morgan, A. M., Truitt, E. B., Jr., and Little, J. M.: J. ...m. Assn., Sc Ed. 46:374, 1957. 5. O'Doherty, D. S., and Shields, C. D.: J.A.M.A. ... 1958. 6. Pa . H. W.: J.A.M.A. 167:168, 1958. 7. Truitt, E. B., Jr., and Patterson, ...roc. Soc. Exp . Bio. & Med. 95:422, 1957. 8. Truitt, E. B., Jr., Patterson, R. D., ...A. M., and Li le, J. M.: J. Pharm. & Exper. Therap. 119:189, 1957.

...y: Tablets (white, scored), 0.5 Gm., bottles of 50 and 500.

H. ROBINS CO., INC., Richmond 20, Va.

Ethical Pharmaceuticals of Merit since 1878

...mary of four new published clinical studies:

...n Beneficial in 95.6% of Cases of Acute Skeletal Muscle Spasm[1, 2, 5, 6]

CONDITION	NO. PATIENTS	RESPONSE			
...DY 1[1]		"marked"	moderate	slight	none
...keletal muscle spasm secondary to acute trauma	33	26	6	1	—
...DY 2[2]		"pronounced"			
...erniated disc	39	25	13	—	1
...igamentous strains	8	4	4	—	—
...orticollis	3	3	—	—	—
...hiplash injury	3	2	1	—	—
...ontusions, fractures, and muscle soreness due to accidents	5	3	2	—	—
...DY 3[5]		"excellent"			
...erniated disc	8	6	2	—	—
...cute fibromyositis	8	8	—	—	—
...orticollis	1	—	—	1	—
...DY 4[6]		"significant"			
...yramidal tract and acute myalgic disorders	30	27	—	2	1
...OTALS	138	104 (75.3%)	28 (20.3%)	4	2

THE JOURNAL of the American Medical Association

"In the author's clinical experience, methocarbamol has afforded greater relief of muscle spasm and pain for a longer period of time without undesirable side effects or toxic reactions than any other commonly used relaxants . . ."[2]

THE JOURNAL of the American Medical Association

"An excellent result, following methocarbamol administration, was obtained in all patients with acute skeletal muscle spasm."[5]

THE JOURNAL of the American Medical Association

"In no instance was there any significant reduction in voluntary strength or intensity of simple reflexes."[6]

Southern Medical Journal

"This study has demonstrated that methocarbamol (Robaxin) is a superior skeletal muscle relaxant in acute orthopedic conditions."[1]

in 1957 and $23 earlier this year, the stock at $37½ should provide a rewarding investment over the longer term.

The company provides natural gas service in three distinct areas of New Jersey, including portions of Morris County in the north central part of the state, a central region from Atlantic Highlands south to Tuckerton and Beach Haven and Cape May County at the extreme southern end of the state. The territory has shown steady economic growth in recent years, with residential, commercial and industrial expansion above average. This has been reflected in a strong upward trend in the company's operating revenues, which have increased from just under $8.2 million for the fiscal year ended September 30, 1953 (the first full year of present operations), to almost $12.5 million for the fiscal year ended September 30, 1957, or by almost 53 per cent.

Substantially the greater part of the revenues, about 83 per cent, is derived from sales to residential customers and in this area the increase in space heating sales has been a major factor in revenue gains. As of September 30, 1957, the house heating saturation level was 27.1 per cent, indicating considerable room for further growth in space heating sales. The territory served by the company includes residential areas within commuting distance of New York City, Newark, Camden and Philadelphia, and other communities devoted to manufacturing, industrial research, quarrying and commercial enterprises, military establishments and relatively large areas devoted to farming, poultry raising, truck farming and fruit growing. The principal manufacturing and quarrying enterprises produce asbestos and insulating materials, ceramics, chemicals, clay products, crushed stone, fertilizer, floor coverings, fine paper, food products, gravel, ice, metal products, paint, paper containers, pharmaceutical supplies and sand. The principal agricultural products are eggs, fruits, vegetables and poultry. The service area of the company also includes the vacation and resort areas located principally along the Atlantic seaboard, the population of which varies between summer and winter seasons, with the summer population being substantially greater than the permanent population. However, the ratio of the extremes is rapidly decreasing.

The company as presently constituted only dates back to June, 1952, when it substantially expanded its operations by acquiring the gas property of Jersey Central Power & Light Company. The meaningful earnings record, therefore, only dates back to 1953. Over this period, operating revenues have shown a strong upward trend, with per share earnings on the common stock increasing at an even more rapid rate. Thus, over this period, earnings per share have risen from 57¢ in 1953 to $1.59 in 1954, and $1.79 in 1955, $2.11 in 1956, $2.29 in 1957 and to $2.67 for the twelve months ended March 31, 1958. During this period, operating revenues have increased by almost 71 per cent, while earnings for the common stock have increased almost 40 per cent. This very substantial rise in common stock earnings largely reflects the high degree of leverage in the income account and the very low carry-through in 1953.

While we believe that earnings can be expected to continue to rise as the company's business grows, it is not

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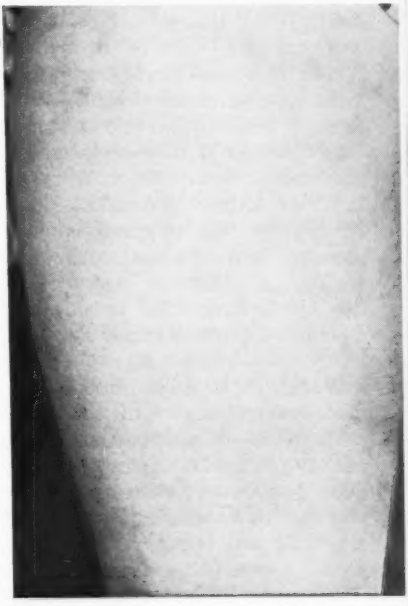
BEFORE USE OF RIASOL



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Many physicians have reported to us the same satisfactory results from the treatment of severe and obstinate cases of psoriasis with RIASOL.*

Itching is relieved immediately, the scales begin to disappear in a few days, the red skin patches gradually fade away, and recurrences are infrequent when the treatment is continued.

RIASOL contains no steroids and adverse reactions have not been reported.

It is a scientifically formulated skin alterative containing mercury 0.45% (in chemical combination with soaps), phenol 0.5% and cresol 0.75%. Applied once daily, at night, by rubbing a thin film in gently after cleansing the skin. No bandages needed.

Supplied in 4 and 8 fld. oz. bottles at pharmacies or direct.

*T. M. Reg. U. S. Pat. Off.

One Trial Will Convince You

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RIASOL FOR PSORIASIS

New Jersey Natural Gas Company			
Price	37½	Capitalization (9/30/57)	
Dividend	$1.60	Long-term Debt	$13,250,000
Yield	4.3%	Preferred Stock	
Traded	O.T.C.	($21.20 par)	104.000 shs
		Common Stock	440,000 shs

likely that per share results will continue to increase at anywhere near as fast a rate as they have over the past few years. Thus earnings for the twelve months ended June 30, 1958, were reported at $2.70 per share, and for the fiscal year ended September 30th of this year, we expect per share results of close to, or only slightly more than, this figure.

From a regulatory standpoint, it appears that the company is earning a fairly full, although not excessive in our opinion, rate of return. This means that future higher earnings must be supported and justified by additional capital investment, rather than obtained by rate increases. While we expect this investment to be made in order to meet expanding demand for service, the required capital financing, including the probable need for selling additional common stock, can also be expected to slow down the rate of increase in per share earnings.

We think it reasonable to expect that the company will continue its stock dividend policy, since it permits the retention of cash for capital expenditures, and offers positive advantages to investors, particularly individuals, who compose the bulk of the company's shareholders. The company's common stock is currently selling around 37½, approximately 13.8 times the reported earnings of $2.71 for the twelve months ended June 30, 1958, to yield approximately 4.3 per cent on the currently indicated $1.60 annual cash dividend. In addition to the cash dividend, the possibility of an additional stock dividend should be kept in mind. If this is retained by investors, it will increase the number of shares owned, and thus future cash dividends to be received will be greater.

In our opinion, the stock is rather fully priced at the present time in relation to our estimate of its basic investment value, which we would place at about $28 to $34. By this term, we mean that value which would be supported by applying normal or average price-earnings ratios to that level of per share earnings (in this case about $2.25) before the company would, in our opinion, be in a position to ask for higher rates. This basic investment value can, we think, be considered as relatively conservative, assuming a continuation of generally favorable economic conditions. It does not take into consideration expectable future growth or increase in earnings and essentially represents a defensive rather than a prospective earnings appraisal.

From a growth standpoint, we think it reasonable to expect increased earnings as the demand for gas service expands, although as indicated above, not at as rapid a rate as shown in the past few years. Over a period of time, higher earnings should permit higher dividends and a gradually rising value for the stock.◀

NEW PHARMACEUTICALS

Daranide *(Merck Sharp & Dohme)*

Oral carbonic anhydrase inhibitor. Each tablet contains 50 mg. of dichlorphenamide. *Indications:* For the treatment of glaucoma. Reduces intraocular pressure. For preoperative control of intraocular tension of glaucoma. *Dosage:* Usual adult dose is 25 to 100 mg. (½ to 2 tablets) 1 to 3 times daily. *Supplied:* In bottles of 100 tablets.

Influenza Virus Vaccine *(Pfizer)*

Two types. Monovalent Type A: each cc. contains 400 CCA units of Asian Strain. Polyvalent Types A & B: each cc. contains 500 CCA units as: Asian Strain, 200 CCA units; Great Lakes Strain, 100 CCA units; PR-8 Strain, 100 CCA units; PR-301 Strain, 100 CCA units. *Supplied:* Each type in vials containing 5 cc. of the vaccine.

Salundek Solution *(Maltbie)*

Antifungal preparation. *Indications:* Ringworm of the scalp. Destroys accessible spores and forms a protective coating over the infected areas, reducing the likelihood of spread of the disease to other areas of the patient's scalp, or to other children. Has no effect on hair growth. *Supplied:* In 3 ounce bottles with controlled flow applicator cap.

Parafon and Parafon with Prednisolone *(McNeil)*

Each compressed tablet contains 125 mg. of chlorzoxazone and 300 mg. of acetaminophen, alone or in combination with 1.0 mg. of prednisolone. *Indications:* For arthritic and rheumatic disorders such as rheumatoid arthritis, rheumatism, myositis, neuritis, tenosynovitis, fibrositis, bursitis, spondylitis and osteoarthritis. For relief of pain, stiffness and limitation of motion associated with disorders involving skeletal muscle spasm. *Dosage:* As directed by the physician. *Supplied: Parafon* in bottles of 50 tablets. *Parafon with Prednisolone* in bottles of 36 tablets.

Prednis-C.V.P. *(Arlington)*

Adrenocortical capillary-protectant therapy. Each capsule contains 4 mg. of prednisolone, 100 mg. of water-soluble citrus bioflavonoid complex, 100 mg. of ascorbic acid, 100 mg. of aluminum hydroxide and 100 mg. of magnesium oxide. *Indications:* For use in rheumatoid arthritis, bronchial asthma, hay fever, inflammatory and allergic skin and eye disorders and other prednisolone-amenable conditions. *Dosage:* Average initial dose, 2 to 5 capsules daily in divided doses. *Supplied:* In bottles of 30, 100 and 500 capsules.

Uro iotic *(Pfizer)*

Bro d-spectrum antibiotic potentiated ith glucosamine. Each capsule con ins 125 mg. of oxytetracycline hyd ochloride with glucosamine, 250 mg. of sulfamethizole and 50 mg. of phe ylazo-diamino-pyridine. *Indicatio* : For the treatment of genito-uri ary infections caused by susceptible organisms. As a prophylactic age t before or after genito-urinary sur ery or instrumentation. *Dosage:* As directed by physician. *Supplied:* In ottles of 50 capsules.

Mi- Cebrin T *(Lilly)*

Oral preparation of therapeutic potency containing multiple vitamins and minerals. *Indications:* In the treatment and prevention of vitamin-mineral deficiencies. An aid to faster recovery following surgery, febrile diseases, severe burns or injuries, or any prolonged convalescence. Especially useful in geriatrics. *Dosage:* One or more tablets daily as needed. *Supplied:* In bottles of 30, 100 and 1,000 tablets.

Metamine Sustained with Reserpine or Butabarbital *(Leeming)*

Each tablet contains 10 mg. of aminotrate phosphate in a sustained release matrix, with either 0.1 mg. of reserpine or ¾ gr. of butabarbital. Exerts 12 hours of protection. *Indications:* To reduce the frequency and severity of attacks of angina pectoris associated with hypertension, and emotional or nervous stress. Reserpine provides gentle, persistent lowering of mean arterial pressure. *Dosage:* One tablet on arising and 1 before the evening meal. *Supplied:* Each form is supplied in bottles of 50 tablets.

Nesacaine with Epinephrine *(Maltbie)*

Local anesthetic. The 1% and 2% strengths are available with epinephrine in 1:100,000 ratio for infiltration, field ,and regional block. The 3% strength available with epinephrine in 1:200,000 ratio for caudal and epidural block. *Supplied:* The 1% and 2% strengths in 30 cc. multiple-dose vials. The 3% strength in 30 cc. single-dose vials.

Engran Baby Drops *(Squibb)*

Nutritional supplement in drop-dosage form for infants and children. Contains nine essential vitamins including B_{12}. *Indications:* As a vitamin supplement. *Dosage:* As determined by physician. *Supplied:* In 15 and 50 cc. bottles with a Flexidose dropper.

Blessamin *(Marvin R. Thompson)*

Comprehensive phosphorous free prenatal vitamin and nutritional supplement. *Indications:* Nutritional supplement during pregnancy. *Dosage:* Usual dosage is 3 capsules daily during meals. *Supplied:* In apothecary jars containing 90 or 240 capsules.

Nitrillin *(Paul Maney)*

Each tablet contains 0.4 mg. of nitroglycerin, 15 mg. of pentaerythritol tetranitrate and 100 mg. of neothylline. *Indications:* In the management of angina pectoris, coronary insufficiency with angina, coronary spasm with myocardial pain, hypertension with angina and anginal syndrome. *Dosage:* As determined by physician. *Supplied:* In bottles of 100 and 1000 tablets.

Uro biotic *(Pfizer)*

Bro d-spectrum antibiotic potentiated vith glucosamine. Each capsule con ains 125 mg. of oxytetracycline hyc ochloride with glucosamine, 250 mg of sulfamethizole and 50 mg. of phe ylazo-diamino-pyridine. *Indicatio :* For the treatment of genitouri ary infections caused by susceptible organisms. As a prophylactic age t before or after genito-urinary sur ery or instrumentation. *Dosage:* As directed by physician. *Supplied:* In ottles of 50 capsules.

Mi Cebrin T *(Lilly)*

Or l preparation of therapeutic potency containing multiple vitamins and minerals. *Indications:* In the treatment and prevention of vitamin-mineral deficiencies. An aid to faster recovery following surgery, febrile diseases, severe burns or injuries, or any prolonged convalescence. Especially useful in geriatrics. *Dosage:* One or more tablets daily as needed. *Supplied:* In bottles of 30, 100 and 1,000 tablets.

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Nesacaine with Epinephrine *(Maltbie)*

Local anesthetic. The 1% and 2% strengths are available with epinephrine in 1:100,000 ratio for infiltration, field ,and regional block. The 3% strength available with epinephrine in 1:200,000 ratio for caudal and epidural block. *Supplied:* The 1% and 2% strengths in 30 cc. multiple-dose vials. The 3% strength in 30 cc. single-dose vials.

Engran Baby Drops *(Squibb)*

Nutritional supplement in drop-dosage form for infants and children. Contains nine essential vitamins including B_{12}. *Indications:* As a vitamin supplement. *Dosage:* As determined by physician. *Supplied:* In 15 and 50 cc. bottles with a Flexidose dropper.

Blessamin *(Marvin R. Thompson)*

Comprehensive phosphorous free prenatal vitamin and nutritional supplement. *Indications:* Nutritional supplement during pregnancy. *Dosage:* Usual dosage is 3 capsules daily during meals. *Supplied:* In apothecary jars containing 90 or 240 capsules.

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Heparin Sodium Solution in *Abboject* Disposable Syringe *(Abbott)*

New product form. Each 1 cc. *Abbojject* disposable syringe contains 20,000 U.S.P. units of heparin sodium. *Indications:* For long-term anticoagulant therapy. *Dosage:* In thrombosis or embolism, 20,000 units administered intramuscularly or subcutaneously provides repository-like effect for as long as 12 hours. *Supplied:* In 1 cc. *Abbojject* disposable syringe with needle, in boxes of 5.

Cosa-Tetracydin Capsules *(Pfizer)*

Contains glucosamine potentiated tetracycline, a broad spectrum antibiotic, an antihistamine and a combination of ingredients for analgesia. *Indications:* For palliative treatment of common cold symptoms and prevention of secondary complications and infections caused by susceptible organisms. Relieves malaise, headache, muscular cramps, aches, pains and the nasal and pharyngeal discharge that accompany the illness. *Dosage:* Average daily adult dose is 2 capsules four times daily, continued until the symptoms subside—usually 3 to 5 days.

Sardo *(Sardeau, Inc.)*

Specially processed oil that releases microfine globules to make hydrophylic water-in-oil suspension. *Indications:* For relief of dryness, itch, scaling and discomfort in atopic dermatitis, eczematoid dermatitis, contact dermatitis, infantile eczema, senile pruritus, dermatitis medicamentosa, diabetic dry skin. Non-sensitizing. *Dosage:* One bottlecapful poured into a bath tub of warm water used once daily. *Supplied:* In bottles of 4, 8 and 16 ounces.

Prednyl Tablets *(Arlington)*

Each tablet contains 1 mg. of prednisolone, 5 grains of salicylamide, 33.3 mg. of water-soluble citrus bioflavonoid compound, 33.3 mg. of ascorbic acid and 50 mg. of aluminum hydroxide. *Indications:* For prompt relief of pain, muscle spasm, inflammation and swelling in rheumatoid arthritis, fibrositis, osteoarthritis, bursitis and other inflammatory and rheumatoid conditions. *Dosage:* Varies with the severity of the disease and the individual response. Generally the initial dose is 1 to 3 tablets 4 times daily, after meals and at bedtime. Dosage should be reduced gradually to minimum effective maintenance levels, usually 3 to 6 tablets daily in divided doses. *Contraindications:* Those of adrenocortical therapy. *Supplied:* In bottles of 100 and 500 tablets.

Vesprin Emulsion *(Squibb)*

New form. Tranquilizer now available in emulsion form. Each cc. contains the equivalent of 10 mg. of trifluopromazine hydrochloride. *Indications:* Particularly suited for pediatric and adult patients who have difficulty in taking tablets. *Supplied:* In 30 cc. dropper bottles and 120 cc bottles.

Lactazine Deltabs *(Marvin R. Thompson)*

Each deltab contains .085 gm. of sulfadiazine, .083 gm. of sulfamerazine, .083 gm. of sulfamethazine and .324 gm. of magnesium lactate as an alkalinizer. *Indications:* In systemic infections susceptible to sulfonamide therapy. *Dosage:* Eight deltabs initially followed by 4 tablets every 4 hours. *Supplied:* In bottles containing 50 or 250 deltabs.

Mec imide *(Abbott)*

A s nthetic compound that acts on the entral nervous system to countera t barbiturate depression or to restor protective reflexes following admin stration of intravenous barbiturate . *Indications:* As an adjunct to the management of barbiturate intox ation and barbiturate and thiobar iturate anesthesia. *Dosage:* As dir ted by physician. *Supplied:* In ste le 10 cc. ampoules, each containing 50 mg. of the drug dissolved in 10 c. of isotonic saline.

Ac idil *(Burroughs Wellcome)*

An ihistamine. Each tablet contains 2.5 mg. of triprolidine hydrochloride. *Indications:* In the treatment of hay fever, pollenosis, vasomotor rhinitis, pruritus, drug sensitivity, allergic dermatitis. Maximum action is apparent in about 3½ hours and duration of effect is approximately 12 hours. *Dosage:* Adults, 1 tablet 2 or 3 times daily. Children over 2 years of age, ½ tablet 2 or 3 times daily. Infants, ¼ tablet 2 or 3 times daily. *Supplied:* In bottles of 100 tablets.

Kynex Pediatric Suspension *(Lederle)*

Each 5 cc. teaspoonful contains 250 mg. of Kynex sulfamethoxypyridazine. *Indications:* For the treatment of genito-urinary and upper respiratory infections, bacillary dysentaries and surgical and soft tissue infections due to sulfonamide-sensitive organisms. *Dosage:* One teaspoonful for each 20 pounds of body weight, followed by ½ teaspoonful on subsequent days. Should be given immediately after meals. *Supplied:* In 4 ounce bottles.

Complications of Varicose Veins

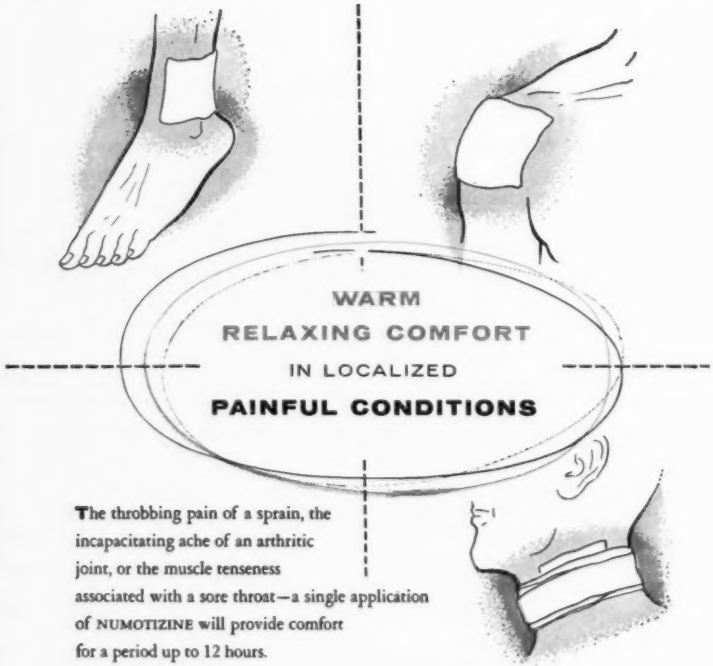
Inflammation of varicosities is frequent even in ambulatory patients. Tender, firm nodules develop in varices which were previously soft and painless. Frequently these patients are put on complete bed rest for weeks or months, with wet compresses and elevation of the involved extremity. Not only is the loss of time unnecessary, but this immobilization is conducive to dangerous deep vein thrombophlebitis. In most cases of superficial phlebitis involving a vein segment below the knee, an elastic bandage will relieve symptoms, allow complete ambulation, and spontanous improvement usually occurs. If severe, anticoagulants or anti-inflammatory agents may be of value. If the phlebitis extends upward in the long saphenous vein toward the groin or if it originates in the upper thigh, a high saphenous vein ligation is indicated. Division of the saphenous vein at the saphenofemoral junction improves the phlebitis and corrects the cause of the varicose veins. This ligation can be performed under local anesthesia in the office.

From a friable superficial varix sudden hemorrhage may follow trivial trauma to the lower leg or foot. Treatment consists of immediate elevation of the affected limb and application of firm pressure over the ruptured vein, then an elastic support to compress the varices, and the patient can be ambulatory. As soon as possible a high ligation and stripping should be done.

The etiology of varicose eczema is often obscure. The eczema usually starts in the malleolar region and spreads, often with a general skin eruption. The treatment is the correction of venous stasis. A gelatin paste boot has proved very effective. For a fungus infection between the toes, potassium permanganate solution 1:5,000 is used. In most cases if the inflamed area is kept clean and dry and stasis corrected the eczema will subside with the patient ambulatory. The boots are changed weekly. If weeping is such that the boot is not tolerated, rubber-reinforced elastic bandages are worn during the day and removed at night.

Varicose ulcer affects 30 to 50 per cent of patients. Each ulcer has a specific cause. Although usually precipitated by trauma, it is the venous stasis which prevents healing.

Bed rest involves loss of time and predisposes to thrombo-embolic complications. If elastic bandages are applied properly, all venous stasis can be controlled. If there is no skin irritation, a four-inch rubber reinforced elastic bandage worn from the toes to the knee is effective. In case of eczema, support may be given by gelatin paste boots aids. No topical therapy is used. Any offending organisms are cultured, and appropriate antibiotic therapy given by injection or or-



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ally. Wet saline dressings are useful. Necrotic tissue is excised. Surgical removal of varicose veins is carried out two or three weeks after complete healing of the ulcer.

Varicose veins and their complications can be controlled while the patient is fully ambulatory. The operative treatment requires only one day in the hospital.

Nabatoff, R. A., *New York J. Med.*, 58:1695-1697, 19[illegible].

Use of *Levonor* for Suppression of Appetite

A group of 80 overweight patients, ranging in age from 15 to 69 years, were given 5 mg. tablets of *Levonor* three times daily ½ hour before meals. Some patients received a fourth dose at 8 or 9 p.m. to curb the night-time snack habit. The average weekly weight loss was two pounds. There were no adverse changes in blood pressure or heart rate. Approximately six per cent of the patients who were accustomed to the lift from the amphetamines were difficult to manage on this therapy, and were considered failures.

Duration of therapy ranged from one to 38 weeks.

Gadek, R. J., et al., *J.A.M.A.*, 167:433-437,1958.

Congestive Heart Failure and the Newer Oral Non-mercurial Diuretics

Of newer oral diuretic preparations, the most potent is chlorothiazide *(Diuril)*, a sulfonamide derivative. The primary effect is a marked increase in sodium and chloride excretion with lesser increase in potassium excretion. Edematous patients refractory to mercurials have shown prompt increase in sodium excretion, with weight losses of 10 to 20 pounds in a 10-day period on 2 gm. a day. A double blind comparison showed chlorothiazide 1 or 2 gm. daily superior to weekly injections of 2 cc. of a potent mercurial diuretic. Chlorothiazide retains its effectiveness during prolonged periods of daily administration in the presence of both acidosis and alkalosis. It also increases sodium excretion in the presence of fairly severe renal insufficiency. But grave electrolyte disturbances may be produced unless the patient is watched carefully during therapy. The most common changes seen are mild hypochloremia, mild hypokalemia, and elevation of plasma bicarbonate. In most patients with no symptoms these reverse themselves when the drugs are discontinued. Because of the dangers of hypokalemia in heart failure, routine administration of potassium has been recommended.

Occasionally there is very marked metabolic acidosis, seen only in patients with mild or moderate renal insufficiency. It is of rather sudden development, with a rising blood urea nitrogen. The degree of renal insufficiency does not seem to be the determining factor, since the majority of patients with renal insufficiency respond with a good diuresis and do not exhibit this disturbance. Hematuria has not been observed. Fairly prompt improvement occurs with cessation of the drug.

Chlorothiazide appears to be the most potent and effective oral diuretic available at present. It promises to be of great value in the management of severe congestive failure and out-patients with heart failure. Patients receiving this drug for prolonged periods should be watched closely for electrolyte disturbances.

Walker, W. G., *Maryland M.J.*, 7:380,1958.

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The Serum Glycoprotein as an Indication of Disease Process

During the last 10 years it has been shown that the serum glycoproteins have considerable significance in clinical chemistry. The major workers in this field have agreed to the following definitions: serum glycoprotein—the total protein-bound carbohydrate found in serum (called serum polysaccharide by many workers); seromucoid—that portion of the serum glycoproteins which is not precipitated with perchloric acid and is precipitated with phosphotungstic acid.

All of the serum globulins contain bound carbohydrate and therefore are glycoproteins. The normal level of serum glycoprotein is lowest in the fetus, highest in the elderly. There is no sex difference. It is elevated in late pregnancy.

Striking elevations of both serum glycoprotein and seromucoid occur in cancer, active rheumatoid arthritis, active gout, active rheumatic fever, and tuberculosis; slight elevations occur in degenerative joint disease or in inactive rheumatic fever. There is no elevation in psychogenic rheumatism. Patients with benign tumors exhibit only slight elevation. Other disease conditions which show elevated glycoprotein levels are cholelithiasis, ulcerative colitis, nephrosis, pemphigus, lupus erythematosus, and periarteritis nodosa. Major operations, fractures, and severe burns also cause decided elevations. Elevations do not occur in anemia, diabetes, hyperthyroidism, hypothroidism, hypertension, and pituitary insufficiency.

In general, when the clinical condition of the patient improves, the serum glycoprotein and seromucoid levels fall.

Shetlar, M. R., *J. Oklahoma M.A.*, 51:323-328,1958.

Serum Glutamic-Oxalacetic Transaminase in Acute Myocardial Infarction

For 18 months all patients with the positive or tentative diagnosis of acute myocardial infarction admitted to hospital and all general patients admitted to the wards were studied. Sera from 200 healthy persons were studied.

The patients with diagnosis of acute myocardial infarction made or suspected were divided into:

1. Patients with definite evidence of acute myocardial infarction.

2. Patients with coronary insufficiency and possible acute myocardial infarcts.

3. Patients with overt liver diseases were excluded.

There were 121 patients in group 1, and of these 103 (85.2%) had enzyme levels above the normal. For 89 of these it was feasible to estimate the age of the infarct; 86% of the peak levels were obtained during the first two sampling days. The clinical manifestation most closely correlating with maximum enzyme concentration was fever. In a great majority of cases peak enzyme levels coincided with ST segment elevation and the appearance of pathologic Q waves and only in a few cases with T wave inversion. In 39 cases the electrocardiogram was interpreted as indicating acute infarction before there was significant elevation of enzyme concentration. In 15 there was a secondary rise in serum enzyme, in four it was accompanied by clinical and electrocardiographic evidence for extension of the infarct.

Conclusions are that proper control of laboratory or reactant temperature is necessary to avoid false elevations of SGO-T. Because of the transient nature of SGO-T elevation and the possibility of death in the first hours postinfarction, there will always be a more or less fixed percentage of false negatives. In this series three of the patients with definite infarcts had normal SGO-T levels. A great majority of other negatives could be explained by time factors. No single clinical, laboratory, or electrocardiographic event could be correlated with the period of maximal elevation of SGO-T. There is question as to the validity of the test in distinguishing myocardial infarction from myocardial ischemia. Other conditions, e.g., cerebrovascular accidents, muscle trauma, pulmonary infarctions, congestive failure, or fractures may cause rises in SGO-T.

Rudolph, L. A., et al., *New York J. Med.*, 58:2520-2524,1958.

Salmonella Infections Not So Rare

The incidence of Salmonella infections as indicated by an extensive survey has materially increased in the past few years. Physicians have not fully appreciated the significance of salmonellosis, except for typhoid fever. Salmonella is the etiologic agent in many undiagnosed infections.

Of Salmonella well over 400 species or serotypes are recognized and every one of them is pathogenic for man, other animals, or both. An outbreak of 17 cases of *S. miami* was traced to watermelons which were purchased at one store and contaminated by the knife when they were cut open. Fifty-one infants were infected with two different Salmonellae because the fluid in the water trap of the delivery room resuscitator was contaminated. Several hundred per-

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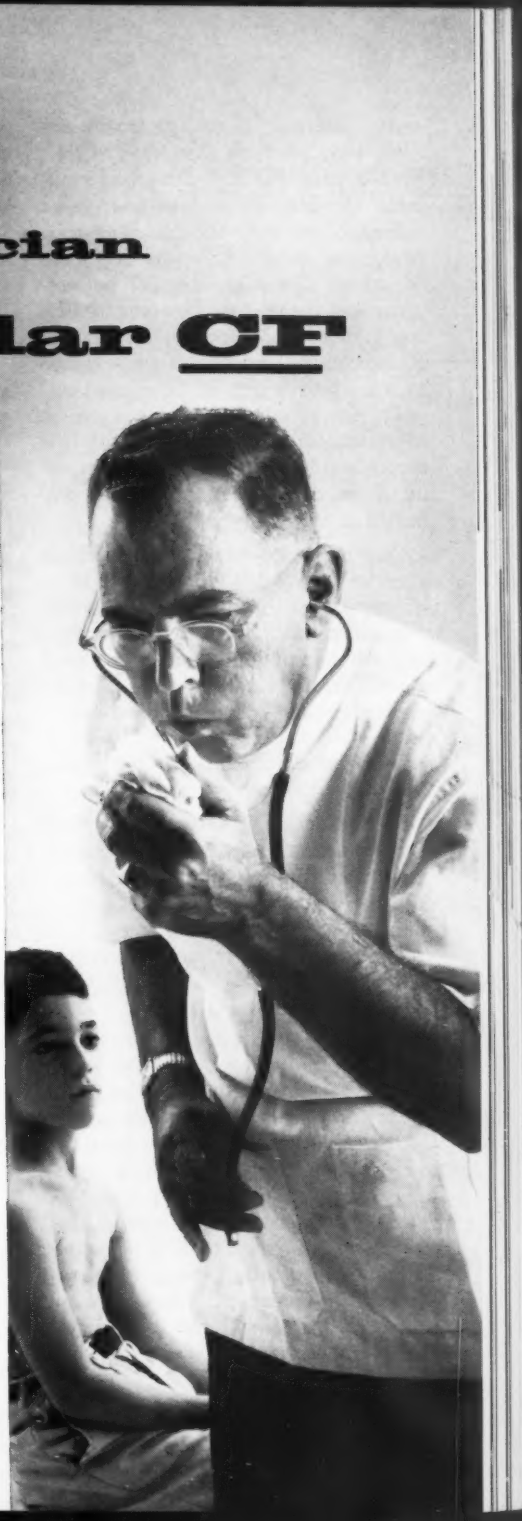

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sons suffered from gastroenteritis after they ate hors d'oeuvres of liver contaminated by one of the food handlers. Contaminated brewer's yeast, a component of a tube feeding mixture, was responsible for five cases of salmonellosis in hospital patients requiring tube feeding for various conditions. Widespread outbreaks of *S. montevideo* infections were traced to a certain brand of powdered egg yolk marketed for infant feeding. More than 500 cases of gastroenteritis throughout the United States caused by *S. reading* were reported in the first five months of 1957.

One way in which salmonellosis may be brought under control is to bring such cases to the attention of physicians and surgeons in active practice. Salmonella infection may present itself in the guise of various medical and pseudo-surgical syndromes. It is dangerous to limit the search for Salmonella to the stool, blood and urine.

Of five cases of "unusual" Salmonella infection from the records of one hospital in a 10 month period, all cultures were isolated by inoculating the specimen submitted to the laboratory on a battery of media. Identification was accomplished by group-specific typing sera.

These five, but a few of the many cases from the records available, well point out the ubiquity of Salmonellae. Salmonella must be considered among the possible causes in any type of bacterial infection—a simple abscess, meningitis, endocarditis, pelvic inflammatory disease, pneumonia, urinary tract infections, etc. Suspecting Salmonella infection only in cases showing gastroenteritis, typhoidal or septic syndrome will continually fall short of revealing the extent, and diversity of salmonellosis. The diagnosis may be difficult and complex clinically and by laboratory. But any microbiology laboratory should be able to identify a Salmonella infection when suitable specimens are submitted.

Balows, A., *J. Kentucky M.A.*, 56:770-773,1958.

Noninflammatory Diseases of Smaller Arteries and Arterioles

Changes characteristic of hypertension occur in the cutaneous blood vessels of patients who have essential hypertension which are similar to those known to be present in the arterioles of the ocular fundi, pectoral muscles, kidneys and other structures and organs of the body. In coarctation of the aorta, hypertensive vascular changes have been noted of equal degree in skin from the calf and from the arm.

A group of diseases of somewhat similar histologic changes in the arterioles include acrocyanosis, livedo reticularis, chronic pernio and hypertensive ischemic ulcers of the leg. The predominant histologic changes are varying degrees of arteriolar spasm and sclerosis.

Acrocyanosis is characterized by persistent blueness and coldness of the hands and feet. Usually it is primary, occasionally secondary to pulmonary osteoarthropathy. Trophic changes and gangrene do not occur, ulceration is rare and usually results from local trauma. Because of the blueness, many patients are concerned and some fear gangrene.

In most cases telling the patient the condition is not likely to give any severe disability suffices. Excessive sweating may require sympathectomy.

Hines, E. A., Jr., *Minnesota Med.*, 41:223-225,1958.

briefs: SURGICAL

Primary Omental Torsion

Primary omental torsion is a partial or complete twisting of the omentum, not associated with adhesions, hernias, or inflammatory conditions. The symptoms depend on the amount of interference with the omental blood supply, and the final stage is gangrene of the distal portion of omentum. The condition develops mainly in obese men.

Three cases of primary omental torsion are reported. Each case closely simulated acute appendicitis and was treated by immediate operative resection of the gangrenous portion of the omentum, with complete cure. Primary omental torsion is rare, but should be looked for within the abdomen when no other pathologic condition is found to explain the other symptoms.

Grant, J. J., & Goehring, W. O., *Pennsylvania M.J.*, 61:1003-1005,1958.

Mitral Valvuloplasty in Patients Past Fifty

Cases of 154 patients with mitral stenosis between the ages of 50 and 70 at the time of surgical correction of this lesion are reviewed and compared with a larger group of patients below this age. Preoperative arterial embolization, associated arteriosclerotic heart disease and elevated blood pressure were all significantly more common in the older group.

Despite these adverse factors, assessment after an average of 25.7 months reveals that, when similar stages of disease are compared, the operative risk, frequency of late death and percentage of improvement after operation are practically identical with those found at younger ages. It may be concluded, therefore, that the properly selected patient over the age of 50 who has mitral stenosis should be offered surgical relief with the same assurance that is justifiable at an earlier age.

Black, H., & Harken, D. E., *New England J. Med.*, 259:361-365,1958.

Intravenous Pethidine in Minor Surgical Procedures

Pethidine has been used intravenously as the sole anesthetic in various painful minor surgical procedures, in gastroscopy, bronchoscopy and cystoscopy.

Its greatest value has been in sigmoidoscopy. Abolition of all afferent pain paths may lead to overdistension of the bowel and perforation, especially if the bowel is fixed and angulated with diverticulitis. Pethidine relaxes the anal sphincter, and inhibits the painful bowel contractions that ensue after distension of the bowel with air, assisting the passage of the instrument. Overdistension or rough pressure with the sigmoidoscope still produces warning pain, but unless the bowel is fixed the

instrument can be passed with a minimum of pain and distress even in the most apprehensive patients. Preliminary injection of scopolamine has been omitted recently in patients being examined in the out-patient department, avoiding the longer delay in recovery. Instead, 75 mg. of pethidine is given intravenously.

Anesthesia of the urethra can be achieved by the use of xylocaine gel, but this requires a laborious technique to get anesthesia of the membranous urethra. Pethidine is now used intravenously, as a preliminary, then the external meatus is cleansed and some gel is squeezed into the urethra and massaged into the posterior urethra. Catheters, sounds and cystoscopes can then be passed with a minimum of discomfort. Many patients who appear for regular dilation now ask for their "injection" to ease the procedure.

The use of intravenous pethidine facilitates the passage of the gastroscope, but diminishes peristaltic action and may cause some misinterpretation of the findings.

A preliminary injection of this drug intravenously facilitates muscular relaxation, acts synergistically with the local analgesic, and appears to prolong its action. It is rare that any additional local analgesic is required. It has been especially suitable for strangulated hernias, suprapubic cystostomies, and for the repair of perforated ulcers in frail and bad-risk cases, and useful in reduction of irreducible hernias.

It does not relax the sphincter of Oddie and so is not effective in controlling the pain of biliary colic. Syncope, hypotension, nausea, vomiting, and vertigo are side-effects that have been ascribed to the use of pethidine.

Markby, C. E. P., *Brit. M.J.*, 1:1397,1958.

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1. Meprobamate is more widely prescribed than any other tranquilizer. Source: Independent research organization; name on request.
2. Baird, H. W., III: A comparison of Meprospan (sustained action meprobamate capsule) with other tranquilizing and relaxing agents in children. Submitted for publication, 1958.

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Antibiotics and Wound Strength

Penicillin exerts its bactericidal effect by interfering with the normal synthesis of bacterial protein. Tetracycline groups may interfere with bacterial synthesis of protein, or they may alter cellular oxidative metabolism. Wounds of patients receiving antibiotics prophylactically in "clean" cases had a higher incidence of skin and fascial dehiscence. An experiment was devised using 30 female rats four to five weeks of age of the Wistar strain. A long left paramedian muscle-splitting incision was made from the left subcostal margin. The peritoneum was opened and then the abdominal wall was closed with through-and-through figure-of-eight sutures, using steel wire.

Ten rats acted as controls, 10 received 5,000 units of crystalline penicillin intramuscularly daily, 10 received 17 mg. of crystalline tetracycline intramuscularly daily. All were on a high-protein, vitamin-supplemented diet with water. The rats were sacrificed on the eighth day.

In wound healing, a stage of fibroplasia follows the initial or lag phase. This is after the sixth day, and because of fibroplasia a wound assumes increasing tensile strength. In the process of fibroplasia, the fibroblasts lay down collagen, a protein, as fibrils. The new fibrils then fuse with those of the periphery as do the proliferating cellular elements. Epithelization may proceed from the edges, followed by the third stage of scar retraction.

This experiment has indicated that the tensile strength of the wounds of rats receiving penicillin and tetracycline was less than that of wounds in rats receiving no antibiotics. There

may be a connection between the impaired protein synthesis of bacteria and the fibroplasia of animals receiving antibiotics.

The control group of albino Wistar female rats which received no antibiotics had the strongest laparotomy wounds.

This study lends another argument against prophylactic use of antibiotics in clean wounds.

Ryan, R. J., *J.M. Soc. New Jersey*, 55:303-304,1958.

Surgery in Arteriosclerosis

When the insidious occlusion of any major vessel progresses to complete cessation of flow, the dependent tissues survive by virtue of the collaterals formed in ratio to the functional need.

This cannot occur in blood vessels which are endpoints in vascular transport, so that anoxia and necrosis occur. Although collaterals may sustain basic anabolic needs, they are inadequate during periods of increased work, and intermittent claudication (which is a painful response of tissues to hypoxia) occurs.

Palpation of the peripheral pulses may prove the most rewarding single procedure in the assessment of major vascular occlusion. The anatomic distribution of pain in claudication is another. Necrotic skin changes project the disease into the terminal vascular bed and obviate restorative surgery. Results of operation will be proportional to the patency of the distal vessels. The mid-popliteal seems to be the endpoint beyond which the salvage can be no more than slight.

If a short segmental obstruction is located in the aorta or in its primary

branches, simple endarterectomy will often suffice. In more extensive involvements, the diseased vessel may be excised and replaced by means of a graft, or a bypass procedure can be performed. The latter now has been shown to have sufficient advantages to warrant its universal application. The technic of bypass is simple, requiring minimal dissection for the establishment of continuity of flow, without disrupting the performed collaterals.

Plastic grafts have proved satisfactory except as replacements for the smaller vessels, for which the lyophilized homografts are superior.

Sympathectomy is not done unless there is an independent reason for it; it has little value in the relief of claudication, and it may upset the circulatory balance by effecting a shunt of blood from the muscular collaterals to the skin.

Murphy, J. P., *J. Iowa M. Soc.*, 48:455-458,1958.

Fat Embolism

Fat embolism occurs in a significant number of cases of traumatic injuries.

During World War II, evidence of fat embolism was found in the lungs of 65 per cent of 60 soldiers who died after various types of battle wounds. In the Korean War it was present in 39 per cent of a group of 79. In a series of 789 accident cases in which there were 125 deaths, 41 of the patients who died had evidence of pulmonary fat embolism, severe enough in 29 cases to be considered the major cause of death.

Fat embolism may or may not be easily recognized. Usually it follows severe crushing injury with fracture of a major long bone. Symptoms in a few minutes or hours are usually those of pulmonary embolization, and may be minimal or severe—dyspnea, hyperpnea, cyanosis and venous distention followed by death. If the patient survives, restlessness, delirium, or coma may appear depending on the severity of systemic embolization. In some cases, marked cerebral symptoms may be present, without premonitory pulmonary signs. The possibility of a head injury must always be considered.

The diagnosis is usually established by the clinical picture and x-ray findings in the chest. Fat droplets in urine are diagnostic, but rarely to be found. Differentiation from intracranial bleeding in cases with deepening coma may be difficult. Head injury and fat embolism may coexist.

In the early stages, fat embolism may also be confused with hemorrhagic shock. Pulmonary blood clot embolism rarely occurs before the 10th day after trauma.

Early, effective splinting of fractures and careful handling of the patient decrease the incidence of fat embolism. Elevation of the injured extremity may lessen the amount of fat entering the circulation. The use of a pneumatic tourniquet has been shown to decrease the amount of fat reaching the lungs if not removed until the limb has been immobilized.

Shock should be treated vigorously with oxygen and adequate blood replacement.

Decholin, a derivative of a bile acid which has both vasodilator and emulsifying properties, may be given safely in doses of 5 ml. of a 20 per cent solution three or four times daily.

Nunn, D. B., & Kredel, F. E., *J. South Carolina M.A.*, 54:233-236,1958.

briefs: THERAPEUTIC

Triamcinolone in the Treatment of Rheumatic Disease

Eighty-nine patients with chronic rheumatic disease were treated with *Aristocort* with good results. The patients required only 80 per cent as much triamcinolone as previously used steroids for the same amount of relief from their symptoms. Twelve patients with active peptic ulcers were treated with the drug, in six of whom healing of the ulcer occurred. There were no psychological disturbances among the 89 patients who were so treated. Although the incidence of side effects was low, the new steroid has not eliminated the possibility of osteoporosis and peptic ulcer attendant upon steroid therapy.

Due to the tendency towards weight loss by patients on this treatment, the drug might be preferred for a patient tending towards edema or for an overweight patient whose appetite is stimulated by other steroids. The steroid is not recommended for an undernourished patient who continues to lose weight.

Freyberg, R. H., et al., *Arthritis & Rheumatism*, 1:7-13,1958.

The Use of *Pacatal* on Ambulatory Patients

A phenothiazine derivative was employed in the treatment of 50 ambulatory patients who were in one of the following diagnostic categories: Arteriosclerotic heart disease, coronary angina, menopausal syndrome, duodenal ulcer, spastic colitis, migraine headache, or senile psychosis. All patients had deep-seated feelings of anxiety, tension and inadequacy.

The initial dose was 25 mg. three times daily, altered to suit the patient's response. No patient was given more than 200 mg. daily, and many were maintained on 25 mg. three times a day.

The drug induced a more normal response to emotional stimuli without producing a sedative or lethargic effect. Aggressiveness and antagonism were subdued, yet the patients remained alert. During treatment, both geriatric and younger patients experienced relief from anxiety, tension and depression. Two especially tense and easily agitated patients with duodenal ulcer responded favorably to the medication.

The only side effect was dryness of the mouth, and this was controlled by decreasing the dosage and then slowly increasing it again.

Darlington, H. F., *Pennsylvania M.J.*, 61:207-208, 1958.

Disturbed Chronic Psychotic Patients: Pilot Trial of Stelazine

In the search for a more efficacious drug with which to treat hospitalized psychotic patients, stelazine (SKK-5019, trifluoroperazine) was given a trial. It had been described as having

nine times the potency of chlorpromazine in blocking conditioned response. Jaundice had not been seen, but extrapyramidal signs and symptoms as in Parkinsonism had been described. Other side-effects noted included rashes, dizziness, drowsiness, lacrimation, and anxiety. The dosage of stelazine was built up gradually over a period of two weeks to 30 mg. daily, in one case to 40 mg., and in another to 45 mg. daily.

A short pilot trial of the drug was undertaken with 25 chronic psychotic patients. Marked side-effects, chiefly of the Parkinson type, were apparent. To these benzhexol hydrochloride gave partial relief.

With the dosage used, the side-effects were so marked and unpleasant that it is doubtful whether the drug would be acceptable for routine use. Higher dosage is unlikely to be helpful in view of the side-effects already encountered. The improvement in a few cases was not sufficient to encourage further use of the drug.

Forrester, M. E., *Brit. M.J.*, 2:90-91,1958.

Intramuscular Iron for Iron Deficiency

An iron-dextran complex given intramuscularly, *Imferon*, was found to be effective as an erythropoietic agent in patients with anemias due to acute and chronic blood loss, post-gastrectomy dumping syndrome, multiple pregnancies, and in essential iron deficiency anemia. The higher concentration of elemental iron in the preparation allows the therapeutic doses to be given in a shorter period of time than intravenously, and the intramuscular route is convenient. Schedule may be maintained on 250 mg. of iron daily without fear of toxic reaction.

Satisfactory clinical results and good hematologic response were obtained in 18 patients with iron deficiency anemia on this medication. Daily doses varied between 100 and 250 mg., and the total dose was 50 mg. of iron for each gm. of hemoglobin deficiency per 100 ml. of blood.

There were no significant local or systemic toxic reactions.

Koszewski, B. J., & Walsh, J. R., *Am. J.M. Sc.*, 235: 523-531,1958.

Effect of Dioctyl Sodium Sulfosuccinate on Bowel Function in Mental Patients

Cramps and straining were eliminated and the number of enemas required by 130 mental patients was reduced when treatment with *Doxinate* was carried out. These were divided into two groups of 66 and 64 patients, respectively. The patients in Group I were given 15 cc. of a one per cent solution in fruit juice before breakfast. After two weeks they received plain orange juice for a period of two weeks.

The patients in Group II were continued on routine cathartics for two weeks, and then were given dioctyl sodium sulfosuccinate for a period of two weeks.

During the first two weeks of treatment all of the patients in Group I passed soft, normal stools within 47 to 72 hours after starting the therapy, the patients in Group II (on cathartics) manifested "fecal rush" and a purgative effect. During the second two weeks the response of the two groups was virtually reversed.

The medication apparently has a predictable efficacy in the management of bowel function in mental patients. There were no significant side effects.

Phelps, D. K., *J. Indiana M.A.*, 51:646-1958.

briefs: OBSTETRIC

Use of Intravenous *Dramamine* to Shorten the Time of Labor and Potentiate Analgesia

Dimenhydrinate reduced pain and induced a sense of tranquility and freedom from apprehension in more than 250 pregnant women. These patients were treated with *Dramamine* by vein, and it was found that the drug both shortened and eased labor. It potentiated the action of analgesic drugs, and in many instances such drugs were unnecessary.

The medication may be given at any stage of labor, but it appears to be especially useful and effective during the latent and acceleration phases. The dose employed was 100 mg. diluted in 10 cc. of water, given intravenously. Slow administration is necessary to prevent elevation of blood pressure, headache, nausea and vomiting. The side reactions of drowsiness, relaxation and sedation which are usually unwanted in ambulatory patients, are desirable qualities during labor.

The average length of labor as compared to that of the controls was shortened by 3.13 hours in the primiparas and 2.7 hours in the multiparas. All phases of cervical dilation were shortened in primigravidas. The drug has a wide margin of safety and no ill effects were reported in either mothers or babies.

Rotter, C. W., et al., *Am. J. Obst. & Gynec.*, 75: 1101,1958.

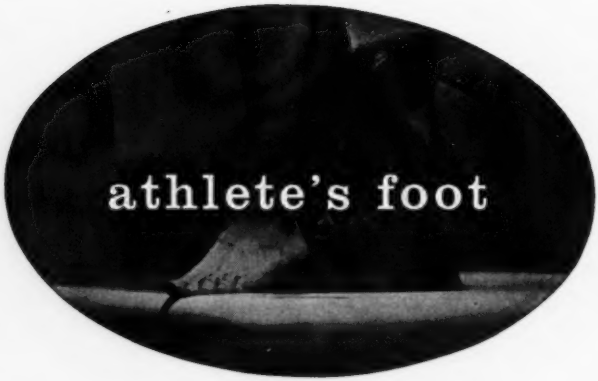
Elective Induction of Labor

It is the prime function and the idealistic aspiration of the obstetrician to diminish the hazards to an irreducible minimum and to make birth as simple and as comfortable as possible, for the woman. A recent artificial supplement to the practice of obstetrics has been the elective induction of labor.

Induction should be limited to the multiparous patient at or near term with a vertex presenting without evidence of disproportion. All technical procedures should be carried out under surgical asepsis.

In the administration of oxytocin, the principal dangers are unsuspected sensitivity of the uterus, too rapid administration and improper dose. The dilution of oxytocin should be standardized at one international unit to each 100 cc. of diluent. Tetanic contractions of the uterus may be avoided either by starting the intravenous drip slowly until the reaction of the uterus has been observed, or by the use of the double-bottle technique. The administration is to be continued throughout the delivery and after the third stage of labor, in order to reduce the possibility of postpartum hemorrhage. Since labor will be short the obstetrician must be in constant and close attendance during the entire induction and labor.

Bishop, E. H., *J.A.M.A.*, 166:1953-1956,1958.



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PD-71

Uterine Rupture After Cesarean Section

The decision to do a cesarean section should be influenced solely by the welfare of the patient. The initial section itself presents few hazards to the mother; the hazards are those of the praevia, abruptio, or dystocia.

Repeat cesarean sections carry with them some increased hazards to mother and infant, especially when general anesthetic agents are used. Further hazard to the baby is failure to correctly appraise the duration of gestation. The premature product of a cesarean section does poorly.

Though it is generally accepted that a patient who once has a section should have a repeat section, it has been reported that 75% of patients in most categories (i.e., toxemia, abruptio, or praevia) who initially have sections could subsequently deliver vaginally; also that 25% of those who initially had sections for cephalic pelvic disproportion could subsequently deliver vaginally. During labors subsequent to cesarean section the doctor must remain with his patient throughout labor.

Cesarean section should be employed only when absolutely indicated, and then the low cervical should be the choice with some few exceptions. The patient who is permitted to deliver vaginally, subsequent to a previous cesarean section, must be attended by her doctor throughout her labor. History of infection or faulty wound healing with or after the initial section contraindicates any attempt at delivery vaginally. A nurse in charge should be taught to report the very first contractions, however insignificant, when the patient in labor has previously had a section.

Wilcox, R. R., *Wisconsin M.J.*, 57:249,1958.

Ergot Poisoning Causing Death in Pregnancy

An unmarried girl of 20 was hospitalized with abortion symptoms. The patient gave a history of vaginal bleeding 12 hours previously. Her last regular menstrual period started 4½ months previously. She had difficulty in breathing for several hours, abdominal pain for 12 hours, and denied having interfered with her pregnancy.

The patient was very pale, restless, and cold to touch. Pulse and blood pressure could not be recorded, breathing was distressed and she was incontinent. Fundal height was that of a pregnancy of 24 weeks. Vaginal examination showed no evidence of bleeding, the cervix felt normal, and the os was closed. Rales and coarse rhonchi could be heard over both lung fields and were loud enough to obscure the heart sounds, which were about 100 beats a minute. The jugular venous pressure was not raised. Shortly after admission the patient had a convulsion and died.

At postmortem both lungs were extremely congested and edematous. Small, dark, firm areas were seen under the pleura, which showed petechial hemorrhages. The heart muscle was flabby. The stomach contained some vegetable matter, the small intestine contained mucus. No evidence of tablets was seen. The uterus was very dark brown, the muscle extremely flabby. The fetus was in intact membranes. There was a small clot and hemorrhagic fluid close to the placenta—100 ml. of blood. All organs were very congested. Ecchymoses were present on the abdominal side of the diaphragm. The uterine muscle was completely necrosed except for a narrow zone of the external layer of fibers 1 mm. wide. The arteries in this area were also necrosed.

Tablets found by the police, as well as in stomach content and various organs at postmortem, contained alkaloids of ergot.

Bridger, M. G., & Rodan, K. S., *Brit. M.J.*, 1:28,1958.

Magnesium Sulfate in Obstetrical Care

Magnesium sulfate in adequate dosage appears to be an excellent drug in the management of severe preeclamptic and eclamptic toxemias, particularly where convulsions are imminent. Often ineffective intramuscular doses of two or three gm. (4 to 6 cc. of 50 per cent solution) are used. To obtain any useful nervous system depression, an initial dose of 8 to 10 gm. is necessary and safe in the 50 to 70 Kg. woman. The drug should be given intramuscle, no more than 2.5 gm. (5 cc. of 50 per cent solution) in any one site. The blood levels obtained will reach their peak in two hours, returning to ineffective levels in four hours. A maintenance dose of 4 to 6 gm. should be given every four to six hours as necessary, but only after the knee jerks are demonstrated. Their absence indicates toxic levels and contraindicates additional drug until they reappear. Loss of the ability to expand the chest on deep respiration indicates serious toxicity and requires calcium gluconate, 1 gm. or more intravenously (10 cc. of 10 per cent solution), an antidote which should always be available. When used in this manner in conjunction with apropriate hypotensive therapy, intramuscular magnesium sulfate is a safe and useful adjunct to therapy for the toxemias of pregnancy.

Peckham, B. M., *Wisconsin M.J.*, 57:206,1958.

Clinical Studies in Culture Conflict

Edited by Georgene Seward, Ph.D., University of Southern California. The Ronald Press Company, New York, N.Y. 1958. $7.00

This volume is designed to fill the need for a case book of clinical studies in culture conflict, which will serve as a diagnostic aid during training and in practice to the clinical psychologist, psychiatrist and social worker in the handling of problems involving culture conflicts. May it serve its purpose.

Orr's Operations of General Surgery

by George A. Higgins, M.D., F.A.C.S., University of Kansas School of Medicine; and Thomas G. Orr, Jr., M.D., F.A.C.S., University of Kansas School of Medicine. Third Edition, with 1990 step-by-step illustrations on 835 figures. W. B. Saunders Company, Philadelphia & London. 1958. $20.00

The author of previous editions succumbed to coronary thrombosis soon after preparation of this edition was begun and the task was completed by two of his students. The plan of the first two editions which made them so popular has been followed out for the third, revising and adding new chapters as progress in surgical knowledge advanced. It is claimed that the information here presented represents the cumulative knowledge and efforts of our surgical forebears through the centuries. It is recognized that the trend toward specialization has so narrowed the field of general surgery as to make it difficult to decide what to include and what to exclude in preparing such a book. One can agree with the claim that the usefulness of a reliable general reference on operations in general surgery remains. An excellent text supplemented by excellent illustrations supplies information on these operations in a way altogether admirable.

Ciba Foundation Symposium: The Cerebrospinal Fluid—Production, Circulation and Absorption

Editors for the Ciba Foundation, G.E.W. Wolstenholme, O.B.E., M.A., M.B., B. Ch.; and Cecilia M. O'Connor, B. Sc. Little, Brown and Company, Boston, Mass. $9.00

It would be difficult to imagine how the symposium's discussion of this subject could have been more elaborate or could have been arranged with a better idea of practical application in the hands of physicians and surgeons.

Physician's Handbook

by Marcus A. Krupp, M.D., Stanford University School of Medicine; Norman J. Sweet, M.D., University of California School of Medicine; et al. Tenth Edition. Lange Medical Publications, Los Altos, California. 1958. $3.00

The 10th edition sustains the character of one of the very best of such handbooks.

Life Insurance and Medicine: The Prognosis and Underwriting of Disease

edited by Harry E. Ungerleider, M.D., F.A.C.P., Director of Medical Research, The Equitable Life Assurance Society of the United States, and Richard S. Gubner, M.D., F.A.C.P., Associate Director of Medical Research, The Equitable Life Assurance Society of the United States; Clinical Associate Professor of Medicine, State University of New York College of Medicine. Charles C. Thomas, Springfield, Ill. 1958. $16.50

This volume is derived from a lecture series conducted under the auspices of The Board of Life Insurance Medicine. Practically everybody accepts the necessity for life insurance. Since it has come to pass that the vast majority of the people of this country, instead of spending today what they made the day before yesterday, spend today what they hope to make the day after tomorrow, this vast majority will pay life insurance premiums with money that they would have spent otherwise, and so made no provision at all for the future.

If life insurance officials and agents would only stop telling folks what is their "duty" and what they "can or cannot afford" to do, and representing themselves as being wholly unselfishly devoted to serving their fellowmen, without thought of gain, I would have no quarrel with them.

The Preservation of Youth: Essay on Health

by Moses Ben Maimon (Maimonides), translated from the original Arabic (Fi Tadbir As-Shihha), with an introduction by Hirsch L. Gordon, M.D., Ph.D., D.H.L. Philosophical Library, New York, N.Y. 1958. $2.75

Anything from Maimonides is well worthy the attention of any doctor of medicine. It is said that "The Preservation of Youth" was written in Arabic in 1198, six years before the death of the author. In addition to directions as to diet and exercise, special regulation of the sex life is urged as a requisite to preservation of full health and vigor of mind and body. The hints that psychological causes may exist for bodily disease accord with a good deal of opinion on that subject today. All through the little book runs evidences of the belief of the author in putting much trust in Nature and mild remedies.

The Medical Assistant

by Miriam Bredow, Eastern School for Physicians' Aides, New York. McGraw-Hill Book Company, Inc., The Blakiston Division, New York, Toronto, & London. 1958. $7.50

Any nurse, secretary, or technician in a doctor's office would do well to purchase and study this book and make daily use of the knowledge there gained.